3/21/05 10/771,824(6)

text search

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CASREACT

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * *

text search

FILE 'HOME' ENTERED AT 10:11:35 ON 21 MAR 2005

α ethyl-2-oxo-1-pyrrolidine-acetamide

=> fil caplus

levetiracetam

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

CAPLUS

FILE 'CAPLUS' ENTERED AT 10:11:46 ON 21 MAR 2005
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2-amino-butanamide

levetiracetam

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+ compositions

2-aminobutyramide

catalyst

one step condensation

FILE COVERS 1907 - 21 Mar 2005 VOL 142 ISS 13
FILE LAST UPDATED: 20 Mar 2005 (20050320/ED)

inventor: Ben-Zion Dolitzky
Jean Hildebrand
Serg. Finogreev

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil casreact

α-aminobutyramide

α-aminobutyric acid amide

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.45	0.66

FILE 'CASREACT' ENTERED AT 10:11:54 ON 21 MAR 2005
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FILE CONTENT:1840 - 20 Mar 2005 VOL 142 ISS 12

****
*
* CASREACT now has more than 8 million reactions *
*
****

Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations

database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s αethyl-2-oxo-1-pyrrolidineacetamide
         90806 ALPHA
             4 ALPHAS
         90807 ALPHA
                 (ALPHA OR ALPHAS)
         52519 ETHYL
             6 ETHYLS
         52524 ETHYL
                 (ETHYL OR ETHYLS)
        369640 2
         23984 OXO
             1 OXOS
         23984 OXO
                 (OXO OR OXOS)
        319996 1
            32 PYRROLIDINEACETAMIDE
             2 PYRROLIDINEACETAMIDES
            32 PYRROLIDINEACETAMIDE
                 (PYRROLIDINEACETAMIDE OR PYRROLIDINEACETAMIDES)
L1           4 AETHYL-2-OXO-1-PYRROLIDINEACETAMIDE
                 (ALPHA(W)ETHYL(W)2(W)OXO(W)1(W)PYRROLIDINEACETAMIDE)

=> s levetiracetam
L2           3 LEVETIRACETAM

=> s L1 or L2
L3           5 L1 OR L2

=> d L3 ibib abs hitstr
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS -------- GI and AB
ALL -------- BIB, AB, IND, RE, Single-step Reactions
APPS ------- AI, PRAI
BIB -------- AN, plus Bibliographic Data
CAN -------- List of CA abstract numbers without answer numbers
CBIB ------- AN, plus Compressed Bibliographic Data
DALL ------- ALL, delimited (end of each field identified)
IABS ------- ABS, indented with text labels
IALL ------- ALL, indented with text labels
IBIB ------- BIB, indented with text labels
IND -------- Indexing data
IPC -------- International Patent Classifications
ISTD ------- STD, indented with text labels
OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

MAX -------- Same as ALL
PATS ------- PI, SO
SCAN ------- TI and FCRD (random display, no answer number.  SCAN
             must be entered on the same line as DISPLAY, e.g.,
             D SCAN.)
SSRX ------- Single-Step Reactions (Map, Diagram, and Summary for
```

all single-step reactions)
STD -------- BIB, IPC, and NCL

CRD -------- Compact Display of All Hit Reactions
CRDREF ----- Compact Reaction Display and SO, PY for Reference
FHIT ------- Reaction Map, Diagram, and Summary for first hit reaction
FHITCBIB --- FHIT, AN plus CBIB
FCRD ------- First hit in Compact Reaction Display (CRD) format
FCRDREF ---- First hit in Compact Reaction Display (CRD) format with CA reference information (SO, PY). (Default)
FPATH ------ PATH, plus Reaction Summary for the "long path"
FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT -------- Reaction Map, Reaction Diagram, and Reaction Summary for all hit reactions and fields containing hit terms
OCC -------- All hit fields and the number of occurrences of the hit terms in each field. Includes total number of HIT, PATH, SPATH reactions. Labels reactions that have incomplete verifications.
PATH ------- Reaction Map and Reaction Diagram for the "long path". Displays all hit reactions, except those whose steps are totally included within another hit reaction which is displayed
RX --------- Hit Reactions (Map, Diagram, Summary for all hit reactions)
RXG -------- Hit Reaction Graphics (Map and Diagram for all hit reactions)
RXL -------- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
RXS -------- Hit Reaction Summariers (Map and Summary for all hit reactions)
SPATH ------ Reaction Map and Reaction Diagram for the "short path". Displays all single step reactions which contain a hit substance. Also displays those multistep reactions that have a hit substance in both the first and last steps of the reaction, except for those hit reactions whose steps are totally included within another hit reaction which is displayed

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of combinations include: D TI; D BIB RX; D TI, AU, FCRD. The information is displayed in the same order as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH, FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may be used with the DISPLAY command to display the record for a specified Accession Number.

ENTER DISPLAY FORMAT (FCRDREF):ibib abs

L3 ANSWER 1 OF 5 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:174073 CASREACT
TITLE: Process for producing **levetiracetam**
INVENTOR(S): Dolityzky, Ben-Zion
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.; Hildesheim, Jean; Finogueev, Serguei
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004069796	A2	20040819	WO 2004-US3149	20040203	
WO 2004069796	A3	20050106			

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004259933	A1	20041223	US 2004-771821	20040203
PRIORITY APPLN. INFO.:			US 2003-444550P	20030203
			US 2003-455795P	20030319

AB **Levetiracetam** is prepared by reaction of (S)-2-aminobutyramide hydrochloride with 4-chlorobutyryl chloride in MeCN or Me tert-Bu ether in the presence of a strong base.

=> ibib abs 2-5
IBIB IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d L3 ibib abs 2-5

L3 ANSWER 2 OF 5 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:170071 CASREACT
TITLE: Preparation of oxopyrrolidine compounds and their use in the manufacture of **levetiracetam** and analogs
INVENTOR(S): Ates, Celal; Surtees, John; Burteau, Anne-Catherine; Marmon, Violeta; Cavoy, Emile
PATENT ASSIGNEE(S): UCB, S.A., Belg.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014080	A2	20030220	WO 2002-EP8717	20020805
WO 2003014080	A3	20031106		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1419144	A2	20040519	EP 2002-764832	20020805

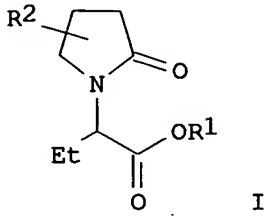
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

JP 2005507378	T2	20050317	JP 2003-519030	20020805
US 2004204476	A1	20041014	US 2004-486342	20040210
PRIORITY APPLN. INFO.:			EP 2001-119396	20010810
			WO 2002-EP8717	20020805

OTHER SOURCE(S): MARPAT 138:170071

GI



I

AB The invention relates to pyrrolidinones I (R1 = Me or Et; R2 = C2-4 alkyl, alkenyl, or alkynyl or their halogen derivs.) as well as (S)-(-)-. **alpha.-ethyl-2-oxo-1-pyrrolidineacetamide** (**levetiracetam**) and to processes for their synthesis. Thus, **levetiracetam** was prepared from (S)-2-aminobutyric acid by alkylation of its Me ester with Et 4-bromobutyrate, cyclization, and amidation.

L3 ANSWER 3 OF 5 CASREACT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 135:210935 CASREACT

TITLE: Process for preparation of 2-oxo-1-pyrrolidine derivatives

INVENTOR(S): Surtees, John; Marmon, Violeta; Differding, Edmond; Zimmermann, Vincent

PATENT ASSIGNEE(S): Ucb Farchim S.A. (Ag - Ltd), Switz.

SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

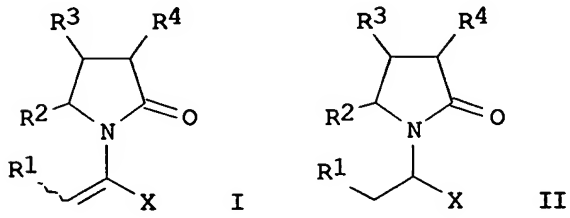
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064637	A1	20010907	WO 2001-EP1956	20010221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2401048	AA	20010907	CA 2001-2401048	20010221
AU 2001073896	A5	20010912	AU 2001-73896	20010221
AU 778510	B2	20041209		
EP 1263727	A1	20021211	EP 2001-940256	20010221
EP 1263727	B1	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001008657	A	20030429	BR 2001-8657	20010221

JP 2003528828	T2	20030930	JP 2001-563480	20010221
EP 1447399	A1	20040818	EP 2004-7733	20010221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EP 1452524	A1	20040901	EP 2004-7878	20010221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EP 1477478	A2	20041117	EP 2004-8270	20010221
EP 1477478	A3	20041124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 282592	E	20041215	AT 2001-940256	20010221
ZA 2002005671	A	20031110	ZA 2002-5671	20020716
ZA 2002005837	A	20031104	ZA 2002-5837	20020722
US 2003040631	A1	20030227	US 2002-204275	20020820
US 6713635	B2	20040330		
BG 107016	A	20030430	BG 2002-107016	20020820
NO 2002003995	A	20021021	NO 2002-3995	20020822
US 2004092576	A1	20040513	US 2003-609544	20030701
US 6858740	B2	20050222		
US 2004192757	A1	20040930	US 2004-824345	20040415
PRIORITY APPLN. INFO.:			GB 2000-4297	20000223
			EP 2001-925354	20010221
			EP 2001-940256	20010221
			WO 2001-EP1956	20010221
			US 2002-204275	20020820
			US 2003-609544	20030701

OTHER SOURCE(S): MARPAT 135:210935

GI



I II

AB 2-Oxo-1-pyrrolidine derivs. (I; X = COOH, COOMe, COOEt, COONH2) were prepared and reacted to give chiral derivs. (II) by asym. hydrogenation in the presence of Rh(I) or Ru(II) catalysts. The invention also concerns a process for preparing α -**ethyl**-2-**oxo**-1-**pyrrolidineacetamide** derivs. from unsatd. 2-oxo-1-pyrrolidine derivs. Particularly the invention concerns novel intermediates and their use in methods for the preparation of (S)-. **alpha.**-**ethyl**-2-**oxo**-1-**pyrrolidineacetamide.**

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 CASREACT COPYRIGHT 2005 ACS on STN

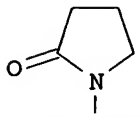
ACCESSION NUMBER: 135:19510 CASREACT

TITLE: Synthesis of α -**ethyl**-[(**2-oxo**)-**1**-]**pyrrolidineacetamide** derivatives

AUTHOR(S): Zhang, Wanjin; Wang, Erhua

CORPORATE SOURCE: Guangdong College of Pharmacy, Canton, 510224, Peop. Rep. China

SOURCE: Guangdong Yaoxueyuan Xuebao (2000), 16(4), 263-264, 270
CODEN: GYXUF8
PUBLISHER: Guangdong Yaoxueyuan
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



Et–CH CONHR I

AB Title compds. I (R = 4-nitrophenyl, 2-methylphenyl, 3-methoxyphenyl, 2,4-difluorophenyl, 3-nitrophenyl) were synthesized from 2-pyrrolidone by substituting with Na 2-bromobutyrate in the presence of NaH, acidifying with HCl to pH 2-3, and acylating with RNH2. The structures were identified by elemental anal., IR, MS spectra, and 1HNMR.

L3 ANSWER 5 OF 5 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 113:191151 CASREACT
TITLE: Preparation of S-α -**ethyl**-**2-oxo-1-pyrrolidineacetamide** via desulfurization/hydrogenolysis
INVENTOR(S): Cossement, Eric; Motte, Genevieve; Geerts, Jean Pierre; Gobert, Jean
PATENT ASSIGNEE(S): UCB S. A., Belg.
SOURCE: Brit. UK Pat. Appl., 9 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2225322	A1	19900530	GB 1989-26244	19891121
GB 2225322	B2	19920325		
NO 8904649	A	19900525	NO 1989-4649	19891122
NO 173823	B	19931101		
NO 173823	C	19940209		
CN 1042904	A	19900613	CN 1989-108764	19891122
CN 1020604	B	19930512		
HU 53072	A2	19900928	HU 1989-6132	19891122
HU 204508	B	19920128		
AT 8902666	A	19901115	AT 1989-2666	19891122
AT 392781	B	19910610		
ES 2023532	A6	19920116	ES 1989-3978	19891122
SU 1797607	A3	19930223	SU 1989-4742434	19891122
PL 161781	B1	19930730	PL 1989-282413	19891122
FI 91961	B	19940531	FI 1989-5562	19891122
FI 91961	C	19940912		
KR 157610	B1	19981116	KR 1989-17038	19891123

PRIORITY APPLN. INFO.: GB 1988-27389 19881123
OTHER SOURCE(S): MARPAT 113:191151
AB The title compound (I), one of the enantiomers of etiracetam known to be useful for treating hypoxic and ischemic assaults on the central nervous

system, is prepared by hydrogenolysis of (S)-α-[2-(methylthio)ethyl]-2-oxo-1-pyrrolidineacetamide (II) with a desulfurizing agent. For example, treating II with Raney Ni T-1 in H2O at 75° gave 69% I. II was prepared either by (a) cyclization of (S)-2-amino-4-(methylthio)butanamide (III) with Cl(CH2)3COCl using KOH and Bu4NBr in CH2Cl2 (61%), or (b) alkylation of III by Et3N and Br(CH2)3CO2Et (35%) and cyclization of the product (36%).

```
=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      27.30      27.96

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -3.40      -3.40

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FILE COVERS 1907 - 21 Mar 2005  VOL 142 ISS 13
FILE LAST UPDATED: 20 Mar 2005  (20050320/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s 2-amino-butanamide
       8326421 2
       1016591 AMINO
            42 AMINOS
       1016608 AMINO
                  (AMINO OR AMINOS)
           600 BUTANAMIDE
            27 BUTANAMIDES
           616 BUTANAMIDE
                  (BUTANAMIDE OR BUTANAMIDES)
L4           0 2-AMINO-BUTANAMIDE
                  (2(W)AMINO(W)BUTANAMIDE)

=> s levetiracetam
L5         244 LEVETIRACETAM

=> s L5 and (butanamid? or butaneamid?)
           659 BUTANAMID?
            10 BUTANEAMID?
L6           6 L5 AND (BUTANAMID? OR BUTANEAMID?)

=> d L6 1-6 ibib abs
```

L6 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:493961 CAPLUS
DOCUMENT NUMBER: 141:47274
TITLE: Methods for identifying a SV2 protein binding partners for the treatment of seizures, neurological diseases, and endocrinopathies
INVENTOR(S): Lynch, Berkley; Nocka, Karl; Fuks, Bruno
PATENT ASSIGNEE(S): UCB, S.A., Belg.
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004051222	A2	20040617	WO 2003-US38122		20031202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004204388	A1	20041014	US 2003-725189		20031202
PRIORITY APPLN. INFO.:			US 2002-430372P	P	20021203
			US 2003-506764P	P	20030930

AB The present invention is drawn to methods of characterization of the properties and functions of SV2 proteins. The present inventors have discovered that SV2A is the binding site for the anti-seizure drug **levetiracetam** (LEV) and its analogs. The high degree of correlation between relative binding affinities of a series of analogs and their anti-convulsant potencies in certain animal models of epilepsy provides strong evidence that binding of these analogs to SV2 proteins modifies their function to provide anticonvulsant effects. The invention further includes methods of identifying binding partners for a SV2 protein, and identifying compds. or agents which modulate the activity of SV2 proteins. Included in these methods is the identification of compds. or agents which modulate the binding of **levetiracetam** to SV2 proteins, including SV2A. The method further comprises determining if the binding of (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl] **butanamide** (LEV analog) to the SV2 protein is inhibited by the potential binding partner, thereby identifying binding partner for the protein. Addnl., the present invention provides biotinylated ligands as a tool to screen chemical libraries and characterize the SV2 proteins. Further, the present invention provides a method of solubilizing and purifying functionally active membrane associated proteins, such as SV2.

L6 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:451561 CAPLUS
DOCUMENT NUMBER: 141:17569
TITLE: Methods for identifying a SV2 protein binding partners, such as **levetiracetam** analogs, for the treatment of seizures, neurological diseases, and endocrinopathies
INVENTOR(S): Lynch, Berkley; Nocka, Karl; Fuks, Bruno
PATENT ASSIGNEE(S): UCB, S.A., USA
SOURCE: U.S. Pat. Appl. Publ., 63 pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004106147	A1	20040603	US 2002-308163	20021203
EP 1426768	A2	20040609	EP 2003-27613	20031202

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: US 2002-308163 A 20021203

AB The present invention is drawn to methods of characterization of the properties and functions of SV2 proteins. The present inventors have discovered that SV2A is the binding site for the anti-seizure drug **levetiracetam** (LEV) and its analogs. The high degree of correlation between relative binding affinities of a series of analogs and their anti-convulsant potencies in certain animal models of epilepsy provides strong evidence that binding of these analogs to SV2 proteins modifies their function to provide anticonvulsant effects. The invention further includes methods of identifying binding partners for a SV2 protein, and identifying compds. or agents which modulate the activity of SV2 proteins. Included in these methods is the identification of compds. or agents which modulate the binding of **levetiracetam** to SV2 proteins, including SV2A. The method further comprises determining if the binding of (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl] **butanamide** (LEV analog) to the SV2 protein is inhibited by the potential binding partner, thereby identifying binding partner for the protein.

L6 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:1011325 CAPLUS
DOCUMENT NUMBER: 140:209928
TITLE: Discovery of 4-Substituted Pyrrolidone **Butanamides** as New Agents with Significant Antiepileptic Activity
AUTHOR(S): Kenda, Benoit M.; Matagne, Alain C.; Talaga, Patrice E.; Pasau, Patrick M.; Differding, Edmond; Lallemand, Benedicte I.; Frycia, Anne M.; Moureau, Florence G.; Klitgaard, Henrik V.; Gillard, Michel R.; Fuks, Bruno; Michel, Philippe
CORPORATE SOURCE: Chemical Research Preclinical CNS Research, and In Vitro Pharmacology, Pharma Sector, UCB S.A., Braine l'Alleud, B-1420, Belg.
SOURCE: Journal of Medicinal Chemistry (2004), 47(3), 530-549 CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB (S)-α-ethyl-2-oxopyrrolidine acetamide 2 (**levetiracetam**, Keppra, UCB S.A.), a structural analog of piracetam, has recently been approved as an add-on treatment of refractory partial onset seizures in adults. This drug appears to combine significant efficacy and high tolerability due to a unique mechanism of action. The latter relates to a brain-specific binding site for 2 (LBS for **levetiracetam** binding site) that probably plays a major role in its antiepileptic properties. Using this novel mol. target, we initiated a drug-discovery program searching for ligands with significant affinity to LBS with the aim to characterize their therapeutic potential in epilepsy and other central nervous system diseases. We systematically investigated the various positions of the pyrrolidone acetamide scaffold. We found that (i) the carboxamide moiety on 2 is essential for affinity; (ii) among 100

different side chains, the preferred substitution α to the carboxamide is an Et group with the (S)-configuration; (iii) the 2-oxopyrrolidine ring is preferred over piperidine analogs or acyclic compds.; (iv) substitution of positions 3 or 5 of the lactam ring decreases the LBS affinity; and (v) 4-substitution of the lactam ring by small hydrophobic groups improves the in vitro and in vivo potency. Six interesting candidates substituted in the 4-position have been shown to be more potent antiseizure agents in vivo than 2. Further pharmacol. studies from our group led to the selection of (2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl]**butanamide** 83α (ucb 34714) as the most interesting candidate. It is approx. 10 times more potent than 2 as an antiseizure agent in audiogenic seizure-prone mice. A clin. phase I program has been successfully concluded and 83α will commence several phase II trials during 2003.

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:787380 CAPLUS

DOCUMENT NUMBER: 140:122643

TITLE: Localization and photoaffinity labelling of the **levetiracetam** binding site in rat brain and certain cell lines

AUTHOR(S): Fuks, Bruno; Gillard, Michel; Michel, Philippe; Lynch, Berkley; Vertongen, Pascale; Leprince, Pierre; Klitgaard, Henrik; Chatelain, Pierre

CORPORATE SOURCE: Braine-l'Alleud, 1420, Belg.

SOURCE: European Journal of Pharmacology (2003), 478(1), 11-19
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Levetiracetam** (2S-(2-oxo-1-pyrrolidinyl)**butanamide**, KEPPRA), a novel antiepileptic drug, has been shown to bind to a specific binding site located in the brain (Eur. J. Pharmacol. 286 (1995) 137). To identify the protein constituent of the **levetiracetam** binding site in situ, we synthesized the photoaffinity label [3H]ucb 30889 ((2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]**butanamide**), a **levetiracetam** analog with higher affinity for the **levetiracetam** binding site. This radioligand was used to map the **levetiracetam** binding site within the brain and to study its cellular and subcellular distribution. Autoradiog. expts. using [3H]ucb 30889 in rat brain revealed a unique distribution profile that did not match that of classical receptors known to be involved in the generation of epileptic seizures. There was a high level of binding in the dentate gyrus, the superior colliculus, several thalamic nuclei, the mol. layer of the cerebellum and to a lesser extent in the cerebral cortex, the striatum and the hypothalamus. The **levetiracetam** binding site was restricted to neuronal cell types, undifferentiated PC12 cells and was highly enriched in synaptic vesicles. [3H]ucb 30889 was also used in photoaffinity labeling studies and shown to bind covalently to a membrane protein with a mol. weight of approx. 90 kDa.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:787379 CAPLUS

DOCUMENT NUMBER: 140:174951

TITLE: Binding characteristics of [3H]ucb 30889 to **levetiracetam** binding sites in rat brain

AUTHOR(S): Gillard, Michel; Fuks, Bruno; Michel, Philippe; Vertongen, Pascale; Massingham, Roy; Chatelain, Pierre

CORPORATE SOURCE: UCB S.A., Braine-l'Alleud, B-1420, Belg.

SOURCE: European Journal of Pharmacology (2003), 478(1), 1-9
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Levetiracetam** (2S-(2-oxo-1-pyrrolidinyl)**butanamide**, KEPPRA), a novel antiepileptic drug, has been shown to bind to a specific binding site located in brain **levetiracetam** binding site. However, [3H]**levetiracetam** displayed only micromolar affinity for these sites making it an unsuitable probe for further characterization. The present study describes the binding properties of an analog of **levetiracetam**: [3H]ucb 30889, (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]**butanamide**. [3H]ucb 30889 binds reversibly to specific binding sites in rat brain. Kinetics at 4°C were biphasic with half-times of association and dissociation of, resp., 3 and 4 min for the fast component and 47 and 61 min for the slow component. [3H]ucb 30889 saturation binding curves were compatible with the labeling of a homogenous population of binding sites having a Bmax of 4496 ± 790 fmol/mg protein (mean ± S.D., n = 5) and a Kd of 62 ± 20 nM (mean ± S.D., n = 5), a 20-fold increase in affinity compared to [3H] **levetiracetam**. Competition binding curves with ligands known to interact with **levetiracetam** binding sites and tissue distribution restricted to the brain indicated that [3H]ucb 30889 and [3H] **levetiracetam** bind to the same site. Although **levetiracetam** binding sites and GABAA (γ-aminobutyric acid) receptors share some ligands such as pentobarbital and pentylenetetrazol, expts. performed with [35S]TBPS (tert-butyl-bicyclo[2.2.2]phosphorothionate), a probe for the GABAA Cl- channel do not support the hypothesis that **levetiracetam** binding sites are part of the GABAA receptor complex. Preliminary autoradiog. studies in rat brain revealed that [3H]ucb 30889 labels specific sites in all brain regions and that this binding is concentration-dependently displaced by **levetiracetam**.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:906159 CAPLUS
DOCUMENT NUMBER: 138:4536
TITLE: 2-Oxopiperidinyl- and 2-oxoazepanylalkanoic acid derivatives for the treatment of epilepsy and other neurological disorders
INVENTOR(S): Michel, Philippe; Kenda, Benoit
PATENT ASSIGNEE(S): Ucb, S.A., Belg.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

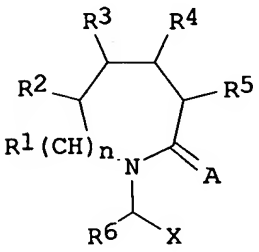
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094787	A1	20021128	WO 2002-EP5503	20020517

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1395560 A1 20040310 EP 2002-740619 20020517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2004132717 A1 20040708 US 2003-476791 20031106
PRIORITY APPLN. INFO.: EP 2001-112541 A 20010523
WO 2002-EP5503 W 20020517

OTHER SOURCE(S): MARPAT 138:4536
GI



I

AB Title compds. I [n = 0, 1; A = O, S; R1-R5 = H, halogen, OH, SH, amino, NO2, N(O), CN, N3, CO2H, carbamoyl, SO3H, aminosulfonyl, alkyl,alkenyl, alkynyl, alkoxycarbonyl, alkoxy, aryl, heterocyclic, acyl, sulfinyl, sulfonyl; R6 = H, (un)substituted alkyl, aryl; X = carbamoyl, (un)esterified CO2H, acyl, CN] were prepared for use as anticonvulsants in the treatment or prevention of epilepsy and other neurol. disorders. Thus, 5-phenyl-2-piperidinone was treated with BrCHEtCO2Et and convert to the amide to give 2-(2-oxo-5-phenyl-1-piperidinyl)**butanamide** (II). The stereoisomers of II were separated and two of them were active at the **levetiracetam** binding site, while the other two were inactive.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d his

     (FILE 'HOME' ENTERED AT 10:11:35 ON 21 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 10:11:46 ON 21 MAR 2005

     FILE 'CASREACT' ENTERED AT 10:11:54 ON 21 MAR 2005
L1             4 S AETHYL-2-OXO-1-PYRROLIDINEACETAMIDE
L2             3 S LEVETIRACETAM
L3             5 S L1 OR L2

     FILE 'CAPLUS' ENTERED AT 10:15:07 ON 21 MAR 2005
L4             0 S 2-AMINO-BUTANAMIDE
L5           244 S LEVETIRACETAM
L6             6 S L5 AND (BUTANAMID? OR BUTANEAMID?)

=> s L5 and composition?
        945219 COMPOSITION?
       1329495 COMPN
        534127 COMPNS
       1627816 COMPN
                 (COMPN OR COMPNS)
       2084838 COMPOSITION?
                 (COMPOSITION? OR COMPN)
L7            19 L5 AND COMPOSITION?
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=> d L7 ibib abs 1-19

L7 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:238949 CAPLUS
TITLE: Process for the preparation of pure **levetiracetam**
INVENTOR(S): Kumar, Yatendra; Prasad, Mohan; Singh, Kaptan; Dhingra, Surender Kumar
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005023763	A1	20050317	WO 2004-IB2850	20040902

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

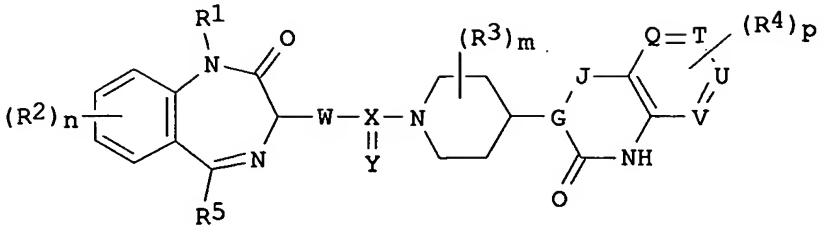
PRIORITY APPLN. INFO.: IN 2003-DE1108 A 20030905
AB The invention relates to processes for the preparation of pure **levetiracetam**. The invention also relates to pharmaceutical **compositions** that include the pure **levetiracetam**.

L7 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:136493 CAPLUS
DOCUMENT NUMBER: 142:240471
TITLE: Preparation of benzodiazepine derivatives as CGRP receptor antagonists
INVENTOR(S): Burgey, Christopher S.; Stump, Craig A.; Williams, Theresa M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005013894	A2	20050217	WO 2004-US20209	20040624

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

SN, TD, TG
PRIORITY APPLN. INFO.: US 2003-482854P P 20030626
GI



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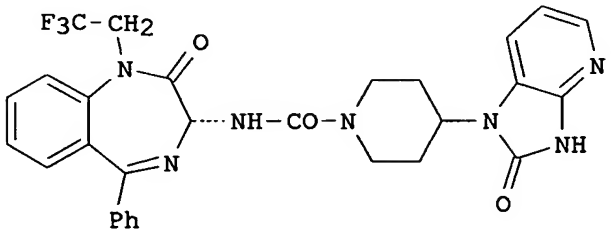

II

AB Benzodiazepine derivs. of formula I [R1 = H, alkyl, cycloalkyl, aryl, etc.; R2 = H, alkyl, cycloalkyl, aryl, etc.; R3 = H, alkyl, CO2H, alkoxycarbonyl; R4 = H, alkyl, cycloalkyl, aryl, etc.; R5 = H, alkyl, cycloalkyl, etc.; n = 1-4; m = 1-9; p = 1-4; W = O, (substituted) NH, (substituted) CH2; X = C, S; Y = O, NCONH2, etc.; G, J = N, NCH2, etc.; Q, T, U, V = CH, N; with provisos] are prepared as antagonists of CGRP receptors, and are useful in the treatment or prevention of diseases in which the CGRP is involved, such as headache, migraine and cluster headache. The invention is also directed to pharmaceutical **compns**. comprising these compds. and the use of these compds. and **compns**. in the prevention or treatment of such diseases in which CGRP is involved. Thus, II was prepared in several steps. The prepared compds. had IC50 values < 50 μM against CGRP receptor.

L7 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:95731 CAPLUS
TITLE: Voltage gated ion channels: Targets for anticonvulsant drugs
AUTHOR(S): Errington, Adam C.; Stoehr, Thomas; Lees, George
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Otago School of Medical Sciences, University of Otago, Dunedin, N. Z.
SOURCE: Current Topics in Medicinal Chemistry (Sharjah, United Arab Emirates) (2005), 5(1), 15-30
CODEN: CTMCCL; ISSN: 1568-0266
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A review. Epilepsy is one of the most prevalent neurol. syndromes in the world today. Epilepsy describes a group of brain disorders whose symptoms and causes are diverse and complicated, but all share a common behavioral manifestation: the seizure. Seizures result from the abnormal discharge of groups of neurons within the brain, usually within a focal point, that can result in the recruitment of large brain regions into epileptiform activity. Although the range of explanations for the development of seizures can be as varied as genetic **composition** to acute head trauma, the net result is often similar. The excitability of neurons is governed by the input they receive from their neighbors and the intrinsic

excitability of the neuron. In this review we focus on elements that are crucial to determining the intrinsic excitability of neurons in the CNS, the voltage gated ion channels (VGICs). VGICs as well as being important for physiol. function are critical in producing hyperexcitability such as that associated with seizure discharges. Many drugs routinely used in the clin. setting, as well as several novel exptl. drugs, have shown interactions with VGICs that underpin, at least in part, their anticonvulsant action. We review the physiol. roles of voltage gated ion channels that are selective for sodium, potassium and calcium conductance and attempt to highlight their role in the pathol. of epilepsy. This is supplemented by the mechanisms of drug action at these important anticonvulsant targets for classical and clin. relevant compds. (e.g. phenytoin, ethosuximide) as well as some important second generation drugs (e.g. Gabapentin, **levetiracetam**) and novel exptl. agents (e.g. Retigabine, Losigamone, safinamide). We also briefly discuss the urgent need for new drugs in this arena and the potential of combinatorial methods and recombinant screening to identify leads.

REFERENCE COUNT: 131 THERE ARE 131 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:14209 CAPLUS
DOCUMENT NUMBER: 142:86677
TITLE: Cyclooxygenase-2 selective inhibitor-anticonvulsant agent combination for the treatment of central nervous system disorders
INVENTOR(S): Stephenson, Diane T.; Taylor, Duncan P.; Arneric, Stephen
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000294	A1	20050106	WO 2004-US17858	20040607

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-476575P P 20030606
OTHER SOURCE(S): MARPAT 142:86677

AB The present invention provides **compns.** and methods for the treatment of central nervous system disorders or related conditions in a subject. More particularly, the invention provides a combination therapy for the treatment of seizures, or seizure disorders comprising the administration to a subject of an anticonvulsant agent in combination with a cyclooxygenase-2 selective inhibitor.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1059117 CAPLUS
DOCUMENT NUMBER: 142:43770
TITLE: Carbostyril derivatives and mood stabilizers for treating mood disorders
INVENTOR(S): Kikuchi, Tetsuro; Iwamoto, Taro; Hirose, Tsuyoshi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004105682	A2	20041209	WO 2004-US13308	20040519

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-473378P P 20030523

AB The pharmaceutical **composition** of the present invention comprises a carbostyril derivative which is a dopamine-serotonin system stabilizer and a mood stabilizer in a pharmaceutically acceptable carrier. The carbostyril derivative may be aripiprazole or a metabolite thereof. The mood stabilizer may include but is not limited to lithium, valproic acid, divalproex sodium, carbamazapine, oxcarbamazapine, zonisamide, lamotrigine, topiramate, gabapentin, **levetiracetam** or clonazepam. These **compns.** are used to treat patients with mood disorders, particularly bipolar disorder with or without psychotic features, mania or mixed episodes. Methods are provided for sep. administration of a carbostyril derivative and a mood stabilizer to a patient with a mood disorder. Thus, a formulation contained dehydroaripiprazole 5, clonazepam 600, starch 131, Mg stearate 4, and lactose 60 mg.

L7 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1015909 CAPLUS
DOCUMENT NUMBER: 142:11552
TITLE: Therapeutic combinations of atypical antipsychotics with GABA modulators and/or anticonvulsant drugs
INVENTOR(S): Romano, Steven Joseph
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004100992	A2	20041125	WO 2004-IB1517	20040503
WO 2004100992	A3	20050120		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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US 2005004106 A1 20050106 US 2004-845826 20040514
PRIORITY APPLN. INFO.: US 2003-471188P P 20030516

AB This invention relates to combinations of (i) an atypical antipsychotic, and (ii) a GABA modulator, a benzodiazepine, and/or an anticonvulsant drug, kits containing such combinations, pharmaceutical **compns.** comprising such combinations, and methods of using such combinations to treat patients suffering from treatment-resistant anxiety disorders, psychotic disorders or conditions, or mood disorders or conditions. For example, a **composition** could be prepared by combining ziprasidone with a GABA modulator, i.e., (a) gabapentin, (b) pregabalin, or (c) lamotrigine, in a pharmaceutically acceptable carrier. The **compn** . contains resp. amts. of ziprasidone and gabapentin, pregabalin or lamotrigine to deliver, on a daily basis about 20 to 160 mg ziprasidone, and about (a) 100 to 400 mg gabapentin; (b) 1 to 500 mg pregabalin; or (c) 2 to 200 mg lamotrigine. The **composition** could be administered to a patient for the treatment of schizophrenia on a daily, twice daily, three times daily, or four times daily basis.

L7 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:902155 CAPLUS
DOCUMENT NUMBER: 141:384286
TITLE: Novel encochleation methods, cochleates and methods of use
INVENTOR(S): Mannino, Raphael J.; Gould-Fogerite, Susan; Krause-Elsmore, Sara L.; Delmarre, David; Lu, Ruying
PATENT ASSIGNEE(S): Biodelivery Sciences International, Inc., USA; University of Medicine and Dentistry of New Jersey
SOURCE: PCT Int. Appl., 195 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091578	A2	20041028	WO 2004-US11026	20040409
WO 2004091578	C1	20050127		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005013854 A1 20050120 US 2004-822230 20040409
PRIORITY APPLN. INFO.: US 2003-461483P P 20030409
US 2003-463076P P 20030415
US 2003-499247P P 20030828
US 2003-502557P P 20030911
US 2003-532755P P 20031224

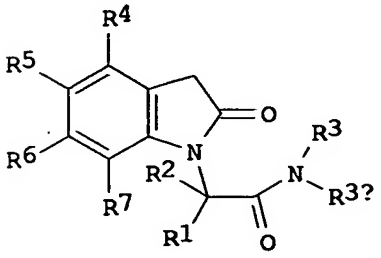
US 2004-537252P P 20040115
US 2004-556192P P 20040324

AB The invention generally relates to cochleate drug delivery vehicles. Disclose are novel methods for making cochleates and cochleate **compns.** that include introducing a cargo moiety to a liposome in the presence of a solvent. Also disclosed are cochleates and cochleate **compns.** that include an aggregation inhibitor, and optionally, a cargo moiety. Addnl., anhydrous cochleates that include a protonized cargo moiety, a divalent metal cation and a neg. charge lipid are disclosed. Methods of using the cochleate **compns.** of the invention, including methods of administration, are also disclosed.

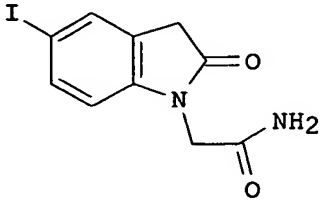
L7 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:857562 CAPLUS
DOCUMENT NUMBER: 141:332048
TITLE: Preparation of indolone-acetamide derivatives, processes for preparing them and their uses
INVENTOR(S): Starck, Jean-Philippe; Kenda, Benoit
PATENT ASSIGNEE(S): Ucb, S.A., Belg.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004087658	A1	20041014	WO 2004-EP2691	20040316
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-7214 A 20030331
OTHER SOURCE(S): MARPAT 141:332048
GI



I



II

AB The present invention relates to indolone-acetamide derivs. I [R1 = H; R2 = H or alkyl; R3 = H, alkyl, cycloalkyl, aryl, etc.; R3a = H, alkyl, (un)substituted heterocyclylalkyl; or R3 and R3a together with the N to which they are attached form a (un)substituted heterocycle; R4 = H, R5 = H, NO2, halo, azido, cyano, alkylthio, alkylsulfinyl; R6 and R7 independently = H, alkyl or halo], processes for preparing them,

pharmaceutical **compns.** containing them and their use as for the treatment of epilepsy, epileptogenesis, seizure disorders and convulsion. Thus, e.g., II was prepared by iodination of 2-(2-oxo-2,3-dihydro-1H-indol-1-yl)acetamide. An assay for determining inhibition consts. of I in competitive binding expts. with **Levetiracetam** is described (no data).

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:799562 CAPLUS
DOCUMENT NUMBER: 141:282837
TITLE: Novel crystalline forms of **levetiracetam**
INVENTOR(S): Parthasaradhi, Reddy Bandi; Rathnakar, Reddy Kura; Raji, Reddy Rapolu; Muralidhara, Reddy Dasari; Subash, Chander Reddy Kesireddy
PATENT ASSIGNEE(S): Hetero Drugs Limited, India
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004083180	A1	20040930	WO 2003-IN58	20030318

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2003-IN58 20030318

AB The present invention relates to novel crystalline forms of **levetiracetam,** to processes for their preparation and pharmaceutical **compns.** containing them. A process for preparation of crystalline forms of **levetiracetam** comprise the steps of (i) mixing **levetiracetam** and a suitable solvent, (ii) maintaining the solution at certain temperature for certain time, and (iii) isolating the crystalline form of **levetiracetam** by ether filtration, or, as in case of water, leaving the solution at room temperature till complete evaporation of water. For example, 10 g of **levetiracetam** was mixed with 50 mL of acetone, heated to reflux., then cooled to 25° to 30° and maintained at this temperature for 2 h. The separated solid was filtered and dried to give 9.0 g of Form I **levetiracetam.**

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:648315 CAPLUS
DOCUMENT NUMBER: 141:179622
TITLE: Controlled release pharmaceutical **compositions** containing polymers
INVENTOR(S): Kannan, Muthaiyyan Esakki; Krishnan, Anandi; Sapre, Beena Amol; Shah, Chitra; Patil, Atul
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004066910	A2	20040812	WO 2004-IB274	20040126
WO 2004066910	C1	20041007		
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
US 2004185097	A1	20040923	US 2004-762180	20040121
PRIORITY APPLN. INFO.:			IN 2003-MU130 A	20030131
			US 2003-517589P P	20031105

AB A solid controlled release pharmaceutical **composition** suitable comprises a drug, a primary release-modifying agent, a secondary release-modifying agent and an auxiliary release-modifying agent, which are present in amts. that synergistically extend the release of the active ingredient. Thus, tablets contained nicotinic acid 500.00, PEG (mol. weight 4,000,000) 170.0, retrograde starch 40.00, lactose monohydrate 30.00, talc 5.00, and Mg stearate 5.00 mg, and water qs.

L7 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:293392 CAPLUS
DOCUMENT NUMBER: 140:297541
TITLE: Neurodegeneration inhibitor, neuroendocrine modulator, and neurocerebral metabolism enhancer
INVENTOR(S): Sassover, Nathan
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004067986	A1	20040408	US 2003-382213	20030305
WO 2004032916	A1	20040422	WO 2003-US29339	20030915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2002-416316P P	20021004
			US 2003-382213 A	20030305

AB Neurometabolic and endocrine function- regulating/modulating **compns.** are disclosed. The **compns.** of the present invention comprise Selegiline Hydrochloride, Procaine Hydrochloride, Vinpocetine, trimethylglycine, and an ingredient selected from a group

consisting of N-nicotinoyl-gamma-aminobutyric acid (N-GABA), niacin, niacinamide, gamma-aminobutyric acid (GABA), and combinations thereof. Methods of using the **compns.**, **compns.**, and **compns.** of the present invention are also disclosed.

L7 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:971868 CAPLUS
DOCUMENT NUMBER: 140:19871
TITLE: Delayed release drug delivery systems containing polymers and method for preparation by mixing and compacting
INVENTOR(S): Hanshermann, Franke; Lennartz, Peter; Raimer, Joern
PATENT ASSIGNEE(S): Desitin Arzneimittel Gmbh, Germany
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101428	A1	20031211	WO 2003-EP5115	20030515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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DE 10224170	A1	20031211	DE 2002-10224170	20020531
BR 2003011512	A	20050222	BR 2003-11512	20030515
EP 1509205	A1	20050302	EP 2003-735396	20030515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: DE 2002-10224170 A 20020531
WO 2003-EP5115 W 20030515

AB The invention relates to a pharmaceutical **composition**, which has a delayed active substance release and can be obtained by means of a special compacting method for which organic solvents and water are not required. Said pharmaceutical **composition** preferably exists in the form of individual active substance compartments or breaks down into compartments of this type when brought into contact with aqueous media. Various types of drugs can be formulated with acrylic copolymers. Thus 30 kg of oxcarbazepine and 9 kg of Eudragit RSPO were mixed in a quick mixer (Diosna P 100); the mixture was compacted using a a Gerteis 3 W-Polygran roller compactor applying 15-40 kN/cm at 80°C. The product was disintegrated by forced sieving and classified through a mash. The particles were encapsulated in hard gel capsules.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:777604 CAPLUS
DOCUMENT NUMBER: 139:271095
TITLE: Preemptive prophylaxis of migraine
INVENTOR(S): Cady, Roger K.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080072	A1	20031002	WO 2003-US7993	20030314
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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CA 2479672	AA	20031002	CA 2003-2479672	20030314
PRIORITY APPLN. INFO.:			US 2002-365691P P	20020318
			WO 2003-US7993 W	20030314

AB A method of preventing the headache phase of migraine in a human comprises administration of an anticonvulsant medication to said human exhibiting prodrome symptoms of migraine. Suitably, the method comprises administration of a migraine headache phase-preventing effective amount of the anticonvulsant. There is also disclosed a pharmaceutical **composition** for the prevention of the headache phase of a migraine containing an anticonvulsant as an active ingredient. There is also disclosed a method of determining prodromal symptoms of migraine using the following cognitive tests: Simple Reaction Time (103); Running Memory Continuous Performance Task (104); Matching to Sample (105); Math. Processing Task (106); and interpreting the results as a percent of baseline indicator of need for prophylaxis.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:319255 CAPLUS
DOCUMENT NUMBER: 138:343854
TITLE: Buccal sprays or capsules containing drugs for treating disorders of the central nervous system
INVENTOR(S): Dugger, Harry A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. Ser. No. 537,118.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003077227	A1	20030424	US 2002-230060	20020829
WO 9916417	A1	19990408	WO 1997-US17899	19971001
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				

EP 1029536	A1	20000823	EP 2000-109347		19971001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
EP 1036561	A1	20000920	EP 2000-109357		19971001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
WO 2004035021	A2	20040429	WO 2003-US26847		20030827
WO 2004035021	A3	20041111			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004141923	A1	20040722	US 2003-671720		20030929
US 2004265239	A1	20041230	US 2003-671715		20030929
US 2004120895	A1	20040624	US 2003-726585		20031204
US 2005002867	A1	20050106	US 2004-834815		20040427
PRIORITY APPLN. INFO.:			WO 1997-US17899	A2	19971001
			US 2000-537118	A2	20000329
			EP 1997-911621	A3	19971001
			US 2002-230060	A	20020829

AB Buccal aerosol sprays or capsules using polar and non-polar solvent have now been developed which provide biol. active compds. for rapid absorption through the oral mucosa, resulting in fast onset of effect. The buccal polar **compns.** of the invention comprise formulation A: aqueous polar solvent, active compound, and optional flavoring agent; formulation B: aqueous polar solvent, active compound, optionally flavoring agent, and propellant; formulation C: non-polar solvent, active compound, and optional flavoring agent; and formulation D: non-polar solvent, active compound, optional flavoring agent, and propellant. Thus, a lingual spray contained sumatriptan succinate 10-15, EtOH 10-20, propylene glycol 10-15, PEG 35-40, water 10-15, and flavors 2-3%.

L7 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2003:291183 CAPLUS
DOCUMENT NUMBER:	139:202670
TITLE:	Microemulsion electrokinetic chromatography applied for separation of **levetiracetam** from other antiepileptic drugs in polypharmacy
AUTHOR(S):	Ivanova, Mariela; Piunti, Alessandra; Marziali, Ettore; Komarova, Natalja; Raggi, Maria Augusta; Kenndler, Ernst
CORPORATE SOURCE:	Institute for Analytical Chemistry, University of Vienna, Vienna, A-1090, Austria
SOURCE:	Electrophoresis (2003), 24(6), 992-998 CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER:	Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Microemulsion electrokinetic chromatog. was applied for the separation of **levetiracetam** from other antiepileptic drugs (primidone, phenobarbital, phenytoin, lamotrigine, and carbamazepine) that are potentially coadministered in therapy of patients. The influence of the **composition** of the microemulsion system (with sodium dodecyl sulfate as charged surfactant) was investigated, modifying the kind of cosurfactant (lower alcs. from C3 to C5), the pH (and salinity) of the aqueous background electrolyte, and the ratio of aqueous phase to organic constituents forming the microdroplets of the oil-in-water emulsion. Separation selectivity was

depending on all these parameters, resulting even in changes of the migration sequence of the analytes. Only moderate correlation was observed for the microemulsion system compared with a micellar system, both consisting of the aqueous borate buffer (pH 9.2) and SDS as micelle former (linear correlation coefficient for analyte mobilities is 0.974). The sample solvent plays an important role on the shape of the resulting chromatograms: MeOH at concns. higher than 35% impairs peak shape and separation efficiency. The microemulsion method (with 93.76% aqueous borate buffer (pH 9.2, 10 mM), 0.48% n-octane, 1.80% SDS, 3.96% 1-butanol, all weight/weight) is suitable for the determination of **levetiracetam** in human plasma (combined with a sample pretreatment based on solid-phase extraction).

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:488246 CAPLUS
DOCUMENT NUMBER: 137:57576
TITLE: Methods and **compositions** using ion-dependent cotransporter modulators for treating conditions of the central and peripheral nervous systems using non-synaptic mechanisms
INVENTOR(S): Hochman, Daryl W.
PATENT ASSIGNEE(S): Cytoscan Sciences L.L.C., USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Ser. No. 470,637.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002082252	A1	20020627	US 2002-56528		20020123
US 6495601	B1	20021217	US 1999-470637		19991222
PRIORITY APPLN. INFO.:			US 1998-113620P	P	19981223
			US 1999-470637	A2	19991222
			US 2001-263830P	P	20010123

AB The invention discloses methods and **compns.** for treating selected conditions of the central and peripheral nervous systems employing non-synaptic mechanisms. More specifically, one aspect of the invention provides methods and materials for treating seizure and seizure disorders, epilepsy, status epilepticus, migraine, spreading depression, intracranial hypertension; for treating the pathophysiol. effects of head trauma, stroke, ischemia and hypoxia; for treating or protecting from the pathophysiol. effects of neurotoxic agents such as ethanol; and for treating neurophsyciatric disorders and central nervous system edema by administering agents that modulate ionic concns. and/or ionic gradients in the brain, particularly ion-dependent or cation-chloride cotransporter antagonists. Electrolyte cotransport antagonists and combinations of such **compns.** with other agents for treating various conditions are disclosed. The invention also discloses methods and **compns.** for treating pain by administering ion-dependent cotransporter antagonists. Methods and **compns.** for enhancing cortical function, e.g. in centers of cognition, learning, and memory, by administering ion-dependent cotransporter agonists are disclosed.

L7 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:525904 CAPLUS
DOCUMENT NUMBER: 135:111992
TITLE: Solid pharmaceutical **compositions** for controlled release of active substances

INVENTOR(S): Fanara, Domenico; Deleers, Michel; Guichaux, Anthony; Berwaer, Monique
PATENT ASSIGNEE(S): Ucb, S.A., Belg.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001051033	A1	20010719	WO 2000-EP13038	20001220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1118321	A1	20010725	EP 2000-100721	20000114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: EP 2000-100721 A 20000114

AB Solid pharmaceutical **compns.** for controlled release of active substances are disclosed. The invention relates to solid pharmaceutical **compns.** which can be administered orally, enabling the controlled release of at least one active substance. The invention also relates to methods for the production of said **compns.** and the uses thereof. A controlled-release tablet contained pseudoephedrin.HCl (I) 240, sodium carbonate 97.5, Natrosol 250 HHX 110, Avicel PH 102 34.8, Aerosil 200 2.7, and magnesium stearate 5 mg. The release of I from the tablets after 20 h was 100.3% at pH = 1.1, and 83.7% at pH = 7.5.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:416774 CAPLUS
DOCUMENT NUMBER: 135:14341
TITLE: Pyrrolidineacetamide derivative, **levetiracetam**, alone or in combination for treatment of CNS disorders
INVENTOR(S): Lamberty, Yves; Matagne, Alain; Klitgaard, Henrik; Waegemans, Tony
PATENT ASSIGNEE(S): Ucb, S.A., Belg.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001039779	A1	20010607	WO 2000-EP11808	20001127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2392879	AA	20010607	CA 2000-2392879	20001127
BR 2000015974	A	20020723	BR 2000-15974	20001127
EP 1244456	A1	20021002	EP 2000-977580	20001127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003515564	T2	20030507	JP 2001-541511	20001127
EE 200200274	A	20030616	EE 2002-274	20001127
AU 773418	B2	20040527	AU 2001-15241	20001127
NZ 518901	A	20040827	NZ 2000-518901	20001127
ZA 2002003690	A	20030819	ZA 2002-3690	20020509
BG 106708	A	20030228	BG 2002-106708	20020516
NO 2002002585	A	20020725	NO 2002-2585	20020531
PRIORITY APPLN. INFO.:			EP 1999-123803 A	19991201
			EP 1999-124269 A	19991201
			WO 2000-EP11808 W	20001127

AB A use of (S)-(-)-α-ethyl-2-oxo-1-pyrrolidineacetamide for the manufacture of a medicament for treatment of particular diseases and new pharmaceutical **compns.** comprising (S)-(-)-α-ethyl-2-oxo-1-pyrrolidineacetamide. **Levetiracetam** is useful for treatment of bipolar disorders, mania, migraine, and chronic or neuropathic pain.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:441913 CAPLUS
DOCUMENT NUMBER: 133:68975
TITLE: Methods and ion-dependent cotransporter antagonist compounds for treating central and peripheral nervous system disorders and methods for screening the compounds
INVENTOR(S): Hochman, Daryl
PATENT ASSIGNEE(S): Cytoscan Sciences L.L.C., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037616	A1	20000629	WO 1999-US30806	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6834238	B1	20041221	US 1999-326244	19990604
CA 2356460	AA	20000629	CA 1999-2356460	19991222
AU 2000023845	A5	20000712	AU 2000-23845	19991222
EP 1141251	A1	20011010	EP 1999-967584	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533353	T2	20021008	JP 2000-589672	19991222
PRIORITY APPLN. INFO.:			US 1998-113620P P	19981223
			US 1999-326244 A	19990604

US 1998-88494P P 19980608
WO 1999-US30806 W 19991222

AB Methods and **compns.** for treating selected conditions of the central and peripheral nervous systems employing non-synaptic mechanisms are described. Examples of the selected conditions are seizure, epilepsy, status epilepticus, migraine, spreading depression, intracranial hypertension; pathophysiol. effects of head trauma, stroke, ischemia and hypoxia; pathophysiol. effects of neurotoxic agents such as ethanol; neuropsychiatric disorders, and central nervous system edema. Treatment comprises administering agents that modulate ionic concns. and/or ionic gradients in the brain, particularly ion-dependent or cation-chloride cotransporter antagonists. Electrolyte cotransport antagonists (e.g., furosemide) and combinations of such **compns.** with other agents are disclosed . Methods and systems for screening drug candidate compds. for desired activities using in vitro and in vivo systems are also described.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> exp dolitzky ben/au 25
E1            1     DOLITZKI BEN ZION/AU
E2            1     DOLITZKI M/AU
E3            0 --> DOLITZKY BEN/AU
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E6            1     DOLITZKY MORDECHAI/AU
E7            4     DOLITZKY YEHUDIT/AU
E8            1     DOLIU O G/AU
E9            1     DOLIVA H/AU
E10           1     DOLIVECK MICHAEL/AU
E11           1     DOLIVEIRA LISA/AU
E12           2     DOLIVEIRA LISA C/AU
E13           1     DOLIVET A/AU
E14           1     DOLIVET ANNE/AU
E15           5     DOLIVET GILLES/AU
E16           1     DOLIVO A/AU
E17           1     DOLIVO BEURET ALLA/AU
E18           1     DOLIVO DOBROVD SKII V V/AU
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E25           1     DOLIVO DOBROVOL SKII V/AU

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             41 "DOLITZKY BEN ZION"/AU
L8           42 ("DOLITZKI BEN ZION"/AU OR "DOLITZKY BEN ZION"/AU)

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E4           10     HILDESHEIM JEFFREY/AU
E5            1     HILDESHEIM K T/AU
E6            4     HILDESHEIM R/AU
E7            8     HILDESHEIM RINA/AU
E8            4     HILDESHEIM W/AU
E9            3     HILDESHEIMER A/AU
E10           1     HILDESHEIMER ARNOLD/AU
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E14           1      HILDESHIEM JEFFERY/AU
E15           1      HILDESSON ASA/AU
E16           1      HILDEWEIN G/AU
E17          12      HILDGEN P/AU
E18          15      HILDGEN PATRICE/AU
E19           1      HILDGEN PATRICE P/AU
E20           1      HILDGENL P/AU
E21           1      HILDGERS PETER/AU
E22           1      HILDHACK W A/AU
E23           1      HILDICK B G/AU
E24           1      HILDICK BRIAN J/AU
E25           1      HILDICK SMITH DAVID J R/AU

=> s e2 or e3
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L9           42 "HILDESHEIM J"/AU OR "HILDESHEIM JEAN"/AU

=> exp finogueev serg/au 25
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E2            3      FINOGINA N P/AU
E3            0 --> FINOGUEEV SERG/AU
E4            2      FINOGUEEV SERGEY/AU
E5           37      FINOGUENOV A/AU
E6            1      FINOGUENOV A V/AU
E7           16      FINOGUENOV ALEXIS/AU
E8            6      FINOIA M G/AU
E9            2      FINOIA MARIA GRAZIA/AU
E10           1      FINOIU VASILE/AU
E11           2      FINOKHIN V I/AU
E12           1      FINOKKUORO P/AU
E13           5      FINOL C/AU
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E15           6      FINOL D/AU
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E17           1      FINOL DORA/AU
E18           3      FINOL DORA M/AU
E19           1      FINOL ENDER ALEXIS/AU
E20           3      FINOL H/AU
E21           5      FINOL H J/AU
E22           2      FINOL HECTOR/AU
E23           4      FINOL HECTOR J/AU
E24           2      FINOL J/AU
E25           1      FINOL JOSE/AU

=> s e4
L10           2 "FINOGUEEV SERGEY"/AU

=> d his

     (FILE 'HOME' ENTERED AT 10:11:35 ON 21 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 10:11:46 ON 21 MAR 2005

     FILE 'CASREACT' ENTERED AT 10:11:54 ON 21 MAR 2005
L1             4 S AETHYL-2-OXO-1-PYRROLIDINEACETAMIDE
L2             3 S LEVETIRACETAM
L3             5 S L1 OR L2

     FILE 'CAPLUS' ENTERED AT 10:15:07 ON 21 MAR 2005
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```
L4            0 S 2-AMINO-BUTANAMIDE
L5          244 S LEVETIRACETAM
L6            6 S L5 AND (BUTANAMID? OR BUTANEAMID?)
L7           19 S L5 AND COMPOSITION?
                EXP DOLITZKY BEN/AU 25
L8           42 S E1,E4
                EXP HILDESHEIM JEAN/AU 25
L9           42 S E2 OR E3
                EXP FINOGUEEV SERG/AU 25
L10           2 S E4

=> s L8 or L9 or L10
L11          83 L8 OR L9 OR L10

=> s L11 and ?iracetam
          1846 ?IRACETAM
L12          0 L11 AND ?IRACETAM

=> s ?iracetam
L13       1846 ?IRACETAM

=> s L13 and amino(6a)butanamide
       1016591 AMINO
            42 AMINOS
       1016608 AMINO
                 (AMINO OR AMINOS)
           600 BUTANAMIDE
            27 BUTANAMIDES
           616 BUTANAMIDE
                 (BUTANAMIDE OR BUTANAMIDES)
            71 AMINO(6A)BUTANAMIDE
L14          1 L13 AND AMINO(6A)BUTANAMIDE

=> d L14 ibib abs

L14  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         1990:591151  CAPLUS
DOCUMENT NUMBER:          113:191151
TITLE:                    Preparation of S-α-ethyl-2-oxo-1-
                          pyrrolidineacetamide via desulfurization/hydrogenolysi
                          s
INVENTOR(S):              Cossement, Eric; Motte, Genevieve; Geerts, Jean
                          Pierre; Gobert, Jean
PATENT ASSIGNEE(S):       UCB S. A., Belg.
SOURCE:                   Brit. UK Pat. Appl., 9 pp.
                          CODEN: BAXXDU
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
     GB 2225322           A1    19900530    GB 1989-26244           19891121
     GB 2225322           B2    19920325
     NO 8904649           A     19900525    NO 1989-4649            19891122
     NO 173823            B     19931101
     NO 173823            C     19940209
     CN 1042904           A     19900613    CN 1989-108764          19891122
     CN 1020604           B     19930512
     HU 53072             A2    19900928    HU 1989-6132            19891122
     HU 204508            B     19920128
     AT 8902666           A     19901115    AT 1989-2666            19891122
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     AT 392781            B     19910610
     ES 2023532           A6    19920116    ES 1989-3978           19891122
     SU 1797607           A3    19930223    SU 1989-4742434        19891122
     PL 161781            B1    19930730    PL 1989-282413         19891122
     FI 91961             B     19940531    FI 1989-5562           19891122
     FI 91961             C     19940912
     KR 157610            B1    19981116    KR 1989-17038          19891123
PRIORITY APPLN. INFO.:                       GB 1988-27389       A  19881123
OTHER SOURCE(S):         CASREACT 113:191151; MARPAT 113:191151
AB   The title compound (I), one of the enantiomers of etiracetam known
     to be useful for treating hypoxic and ischemic assaults on the central
     nervous system, is prepared by hydrogenolysis of (S)-α-[2-
     (methylthio)ethyl]-2-oxo-1-pyrrolidineacetamide (II) with a desulfurizing
     agent.  For example, treating II with Raney Ni T-1 in H2O at 75°
     gave 69% I.  II was prepared either by (a) cyclization of (S)-2-
     amino-4-(methylthio)butanamide (III) with Cl(CH2)3COCl
     using KOH and Bu4NBr in CH2Cl2 (61%), or (b) alkylation of III by Et3N and
     Br(CH2)3CO2Et (35%) and cyclization of the product (36%).


=> s levetiracetam or piracetam or etiracetam
          244 LEVETIRACETAM
         1114 PIRACETAM
           12 ETIRACETAM
L15      1344 LEVETIRACETAM OR PIRACETAM OR ETIRACETAM

=> s L15 and "one step condensation"
      1939847 "ONE"
       156645 "ONES"
      2064925 "ONE"
                ("ONE" OR "ONES")
       399733 "STEP"
       266335 "STEPS"
       618999 "STEP"
                ("STEP" OR "STEPS")
       312634 "CONDENSATION"
         7142 "CONDENSATIONS"
       315667 "CONDENSATION"
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           43 "ONE STEP CONDENSATION"
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L16         0 L15 AND "ONE STEP CONDENSATION"

=> s L15 and "one step"
      1939847 "ONE"
       156645 "ONES"
      2064925 "ONE"
                ("ONE" OR "ONES")
       399733 "STEP"
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       618999 "STEP"
                ("STEP" OR "STEPS")
        20771 "ONE STEP"
                ("ONE"(W)"STEP")
L17         1 L15 AND "ONE STEP"

=> d L17 ibib abs

L17  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2000:554945  CAPLUS
DOCUMENT NUMBER:         133:281668
TITLE:                   Synthesis of 1-azabicyclo[3.3.0]octane derivatives and
                         their effects as piracetam-like nootropics
```

AUTHOR(S): Oka, Mitsuru; Matsumoto, Yukiharu; Hirooka, Kiyotaka; Suzuki, Tomoo

CORPORATE SOURCE: Central Research Laboratory, Sanwa Kagaku Kenkyusho, Co., Ltd., Mie, 511-0406, Japan

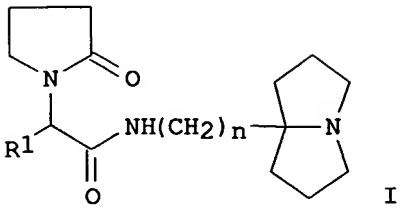
SOURCE: Chemical & Pharmaceutical Bulletin (2000), 48(8), 1121-1124
CODEN: CPBTAL; ISSN: 0009-2363

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB A useful pharmaceutical intermediate, 5-nitromethyl-1-azabicyclo[3.3.0]octane (I), was prepared in **one step** from 1,7-dichloro-4-heptanone under mild conditions. Catalytic hydrogenation of I over Raney Ni in the presence of sodium hydroxide afforded 5-aminomethyl-1-azabicyclo[3.3.0]octane (II) in high yield. **Piracetam** analogs III [R1 = H, Et, Ph; n = 1, 2] were prepared from II or its aminoethyl analog and 2-oxo-1-pyrrolidineacetates. Pharmacol. tests showed that III [R1 = H, n = 1] improves cerebral function.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s L15 and "no catalyst"
       3172572 "NO"
        169246 "NOS"
          1795 "NOES"
       3270879 "NO"
                 ("NO" OR "NOS" OR "NOES")
        683332 "CATALYST"
        686922 "CATALYSTS"
        875909 "CATALYST"
                 ("CATALYST" OR "CATALYSTS")
          1298 "NO CATALYST"
                 ("NO"(W)"CATALYST")
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=> s L15 and "without(3a)catalyst"
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             1 "WITHOUTS"
       1098961 "WITHOUT"
                 ("WITHOUT" OR "WITHOUTS")
         28308 "3A"
        683332 "CATALYST"
        686922 "CATALYSTS"
        875909 "CATALYST"
                 ("CATALYST" OR "CATALYSTS")
             0 "WITHOUT(3A)CATALYST"
                 ("WITHOUT"(W)"3A"(W)"CATALYST")
L19           0 L15 AND "WITHOUT(3A)CATALYST"
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            1 WITHOUTS
      1098961 WITHOUT
                (WITHOUT OR WITHOUTS)
       683332 CATALYST
       686922 CATALYSTS
       875909 CATALYST
                (CATALYST OR CATALYSTS)
        10630 WITHOUT(3A)CATALYST
L20         0 L15 AND WITHOUT(3A)CATALYST

=> s 2-amino-butanamide(3a)hydrochloride
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      1016591 AMINO
           42 AMINOS
      1016608 AMINO
                (AMINO OR AMINOS)
          600 BUTANAMIDE
           27 BUTANAMIDES
          616 BUTANAMIDE
                (BUTANAMIDE OR BUTANAMIDES)
            0 2-AMINO-BUTANAMIDE
                (2(W)AMINO(W)BUTANAMIDE)
       140812 HYDROCHLORIDE
         9287 HYDROCHLORIDES
       145735 HYDROCHLORIDE
                (HYDROCHLORIDE OR HYDROCHLORIDES)
L21         0 2-AMINO-BUTANAMIDE(3A)HYDROCHLORIDE

=> d his

     (FILE 'HOME' ENTERED AT 10:11:35 ON 21 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 10:11:46 ON 21 MAR 2005

     FILE 'CASREACT' ENTERED AT 10:11:54 ON 21 MAR 2005
L1           4 S AETHYL-2-OXO-1-PYRROLIDINEACETAMIDE
L2           3 S LEVETIRACETAM
L3           5 S L1 OR L2

     FILE 'CAPLUS' ENTERED AT 10:15:07 ON 21 MAR 2005
L4           0 S 2-AMINO-BUTANAMIDE
L5         244 S LEVETIRACETAM
L6           6 S L5 AND (BUTANAMID? OR BUTANEAMID?)
L7          19 S L5 AND COMPOSITION?
               EXP DOLITZKY BEN/AU 25
L8          42 S E1,E4
               EXP HILDESHEIM JEAN/AU 25
L9          42 S E2 OR E3
               EXP FINOGUEEV SERG/AU 25
L10          2 S E4
L11         83 S L8 OR L9 OR L10
L12          0 S L11 AND ?IRACETAM
L13       1846 S ?IRACETAM
L14          1 S L13 AND AMINO(6A)BUTANAMIDE
L15       1344 S LEVETIRACETAM OR PIRACETAM OR ETIRACETAM
L16          0 S L15 AND "ONE STEP CONDENSATION"
L17          1 S L15 AND "ONE STEP"
L18          0 S L15 AND "NO CATALYST"
L19          0 S L15 AND "WITHOUT(3A)CATALYST"
L20          0 S L15 AND WITHOUT(3A)CATALYST
L21          0 S 2-AMINO-BUTANAMIDE(3A)HYDROCHLORIDE
```

```
=> s L8 and levetiracetam
           244 LEVETIRACETAM
L22          0 L8 AND LEVETIRACETAM

=> s US20040259933/pn
L23          1 US20040259933/PN
                (US2004259933/PN)

=> d L23

L23  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:675721  CAPLUS
DN   141:174073
TI   Process for producing levetiracetam
IN   Dolityzky, Ben-Zion
PA   Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA,
     Inc.; Hildesheim, Jean; Finogueev, Serguei
SO   PCT Int. Appl., 17 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.      DATE
     --------------      ----   --------    -------------------  --------
PI   WO 2004069796        A2    20040819    WO 2004-US3149       20040203
     WO 2004069796        A3    20050106
         W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
             BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
             CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
             ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
             IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
             LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
             MZ, MZ, NA, NI
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
             MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
     US 2004259933        A1    20041223    US 2004-771821       20040203 <--
PRAI US 2003-444550P      P     20030203
     US 2003-455795P      P     20030319
OS   CASREACT 141:174073


=> d L23 it

L23  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2005 ACS on STN
IT   Molecular sieves
        (drying agent; preparation of levetiracetam)
IT   Drying agents
        (preparation of levetiracetam)
IT   497-19-8, Sodium carbonate, reactions   584-08-7, Potassium carbonate
     7487-88-9, Magnesium sulfate, reactions   7757-82-6, Sodium sulfate,
     reactions
     RL: RGT (Reagent); RACT (Reactant or reagent)
        (drying agent; preparation of levetiracetam)
IT   103765-01-1P, 1-Pyrrolidineacetamide, α-ethyl-2-oxo-, (αR)-
     RL: BYP (Byproduct); REM (Removal or disposal); PREP (Preparation); PROC
     (Process)
        (preparation of levetiracetam)
IT   102767-28-2P, Levetiracetam
     RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN
```

(Synthetic preparation); PREP (Preparation)
(preparation of levetiracetam)
IT 75-05-8, Acetonitrile, uses 1634-04-4, Methyl tert-butyl ether
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of levetiracetam)
IT 4635-59-0, 4-Chlorobutyryl chloride 7682-20-4, (S)-2-Aminobutyramide hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of levetiracetam)

=> s 2-aminobutyramide
8326421 2
80 AMINOBUTYRAMIDE
6 AMINOBUTYRAMIDES
85 AMINOBUTYRAMIDE
(AMINOBUTYRAMIDE OR AMINOBUTYRAMIDES)
L24 10 2-AMINOBUTYRAMIDE
(2(W)AMINOBUTYRAMIDE)

=> d L8 ti,au,so 1-10

L8 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI A recycling process for preparing sertraline
IN Mendelovici, Marioara; **Dolitzky, Ben-Zion**; Etinger, Marina Yu; Nisnevich, Gennady A.
SO PCT Int. Appl.
CODEN: PIXXD2

L8 ANSWER 2 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Method for reducing residual alcohols in crystalline valacyclovir hydrochloride
IN **Dolitzky, Ben-zion**; Lifshitz, Igor
SO U.S. Pat. Appl. Publ., 6 pp., Cont.-in-part of U.S. Ser. No. 688,538.
CODEN: USXXCO

L8 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Crystalline forms of valacyclovir hydrochloride
IN Wizel, Shlomit; Aronhime, Judith; Niddam-hildesheim, Valerie; **Dolitzky, Ben-Zion**; Etinger, Marina Yu; Yuzefovich, Michael; Nisnevich, Gennady; Pertsikov, Boris; Tishin, Boris; Blasberger, Dina
SO U.S. Pat. Appl. Publ., 25 pp., Cont.-in-part of U.S. Ser. No. 236,729.
CODEN: USXXCO

L8 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Crystallization process for purifying and isolating racemic bicalutamide
IN **Dolitzky, Ben-Zion**; Reany, Ofer; Shammai, Jenny
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2

L8 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Process for the preparation of famciclovir
IN Shamai, Genny; Antebi, Shlomo; Ioffe, David; **Dolitzky, Ben-Zion**; Kauffmann, Batia
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2

L8 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Process for the preparation of valsartan
IN Harel, Zvi; Rukhman, Igor; **Dolitzky, Ben-Zion**
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2

L8 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Process for the preparation of valsartan
IN Harel, Zvi; Rukhman, Igor; **Dolitzky, Ben-Zion**; Flyaks, Evgeni; Koltai, Tamas; Aronhime, Judith
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

L8 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Synthesis of quetiapine and pharmaceutically acceptable salts thereof
IN Diller, Dov; **Dolitzky, Ben-zion**
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2

L8 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Synthesis of 2-butyl-3-[[2'-(1-trityl-1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1,3-diazaspiro[4,4]-non-ene-4-one
IN Nisnevich, Gennady; Rukhman, Igor; Pertsikov, Boris; Kaftanov, Julia; **Dolitzky, Ben-zion**
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2

L8 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Synthesis of gatifloxacin
IN Niddam-Hildesheim, Valerie; **Dolitzky, Ben-Zion**; Pilarski, Gideon; Sterimbaum, Greta
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2

=> d L8 ti,au,so 11-42

L8 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Synthesis of irbesartan
IN Nisnevich, Gennady; Rukhman, Igor; Pertsikov, Boris; Kaftanov, Julia; **Dolitzky, Ben-zion**
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2

L8 ANSWER 12 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Methods for the preparation of olanzapine hydrate and solvate crystal forms
IN **Dolitzky, Ben Zion**; Aronhime, Judith; Diller, Dov
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2

L8 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI An improved method of synthesis of 3,5-dihydroxy-7-pyrrol-1-yl heptanoic acids (atorvastatin derivatives)
IN Oren, Jakob; **Dolitzky, Ben-zion**; Harel, Zvi; Perlman, Nurit; Lidor-Hadas, Ramy
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2

L8 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Method for reducing the residual process alcohols present in crystalline valacyclovir hydrochloride by contacting it with a humid gas at ambient pressure
IN **Dolitzky, Ben-Zion**; Lifshitz, Igor
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2

L8 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Crystalline solid famciclovir forms I, II, III and preparation thereof

IN **Dolitzky, Ben-Zion**; Wizel, Shlomit; Reany, Ofer; Shammai, Jenny
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2

L8 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Preparation and crystallization of bicalutamide
IN **Dolitzky, Ben-Zion**; Reany, Ofer; Shammai, Jenny
SO U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 170,721.
CODEN: USXXCO

L8 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Preparation of polymorphic forms of nateglinide
IN Yahalomi, Ronit; Shapior, Evgeny; **Dolitzky, Ben-zion**; Gozlan, Yigael; Gome, Boaz
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2

L8 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Synthesis of irbesartan
IN Nisnevich, Gennady; Rukhman, Igor; Pertsikov, Boris; Kaftanov, Julia; **Dolitzky, Ben-Zion**; Shapiro, Eugeny; Yahalomi, Bonit
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2

L8 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Process for preparing nateglinide and its intermediates
IN Yahalomi, Ronit; Shapiro, Evgeny; **Dolitzky, Ben-zion**; Gozlan, Yigael
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2

L8 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Polymorphic Form XVI of fexofenadine hydrochloride
IN Krochmal, Barnaba; Diller, Dov; **Dolitzky, Ben-Zion**; Aronhime, Judith; Wizel, Shlomit; Gome, Boaz; Lifshitz, Igor
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2

L8 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Processes for preparing losartan by cleavage of triarylmethyl-substituted losartans in liquid ketones and losartan potassium by basification with potassium ions in pure liquid alcohols
IN **Dolitzky, Ben-Zion**
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2

L8 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Crystalline forms of quetiapine hemifumarate
IN Lifshitz-Liron, Revital; Kovalevski-Ishai, Eti; **Dolitzky, Ben-Zion**; Wizel, Shlomit; Lidor-Hadas, Rami
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2

L8 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Fine particle size pioglitazone
IN Samburski, Guy; **Dolitzky, Ben-Zion**
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2

L8 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Catalytic hydrogenation of exocyclic double bonds in production of thiazolidinedione antihyperglycemics
IN **Dolitzky, Ben-zion**

SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2

L8 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Amorphous and crystalline forms of losartan potassium
IN **Dolitzky, Ben Zion**; Weizel, Shlomit; Nisnevich, Gennady; Rukhman, Igor; Kaftanov, Julia
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2

L8 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Synthesis and purification of valacyclovir
IN Etinger, Marina Yu; Yudovich, Lev M.; Yuzefovich, Michael; Nisnevich, Gennady A.; **Dolitzki, Ben Zion**; Pertsikov, Boris; Tishin, Boris; Blasberger, Dina
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2

L8 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Polymorphs of fexofenadine base
IN Krochmal, Barnaba; Diller, Dov; **Dolitzky, Ben-Zion**; Aronhime, Judith; Wizel, Shlomit
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2

L8 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Crystalline forms of valacyclovir hydrochloride
IN Wizel, Shlomit; Aronhime, Judith; Niddam-Hildesheim, Valerie; **Dolitzky, Ben-Zion**; Etinger, Marina Yu; Yuzefovich, Michael; Nisnevich, Gennady A.; Pertsikov, Boris; Tishin, Boris; Blasberger, Dina
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2

L8 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Polymorphs of fexofenadine hydrochloride
IN **Dolitzky, Ben-Zion**; Wizel, Shlomit; Krochmal, Barnaba; Diller, Dov; Gross, Irwin
SO U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of U. S. Ser. No. 118,807.
CODEN: USXXCO

L8 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Preparation of rac-bicalutamide
IN **Dolitzky, Ben-Zion**; Reany, Ofer; Shamai, Jenny
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2

L8 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Preparation of polymorphs of venlafaxine hydrochloride
IN **Dolitzky, Ben-zion**; Aronhime, Judith; Wizel, Shlomit; Nisnevich, Gennady A.
SO U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Provisional Ser. No. 241,577.
CODEN: USXXCO

L8 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Polymorphs of fexofenadine hydrochloride
IN **Dolitzky, Ben-Zion**; Wizel, Shlomit; Krochmal, Barnaba; Diller, Dov; Gross, Irwin
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2

L8 ANSWER 33 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI New crystal forms of lamotrigine and processes for their preparations

IN Garti, Nissim; Berkovich, Yana; **Dolitzky, Ben-Zion**; Aronhime, Judith; Singer, Claude; Lieberman, Anita; Gershon, Neomi
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2

L8 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Preparation of crystal forms of oxcarbazepine
IN Aronhime, Judith; **Dolitzky, Ben-zion**; Berkovich, Yana; Garth, Nissim
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2

L8 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Crystalline venlafaxine base and novel polymorphs of venlafaxine hydrochloride and processes for their preparation
IN **Dolitzky, Ben-Zion**; Aronhime, Judith; Weizel, Shlomit; Nisnevish, Gennady
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2

L8 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Preparation of risperidone from 3-(2-chloroethyl)-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one and 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole in acetonitrile, isopropanol, methyl ethyl ketone, or isobutanol.
IN Krochmal, Barnaba; Diller, Dov; **Dolitzky, Ben-Zion**
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2

L8 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Micronized torsemide
IN Kordova, Marco; Schwartz, Anchel; **Dolitzky, Ben-Zion**; Aronhime, Judith; Leonov, David; Zavurov, Shlomo; Salyi, Szabolcs; Meszaros-Sos, Erzsebet
SO PCT Int. Appl., 9 pp.
CODEN: PIXXD2

L8 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Preparation of novel polymorphic forms of risperidone
IN Krochmal, Barnaba; Diller, Dov; **Dolitzky, Ben-Zion**; Aronhime, Judith
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2

L8 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Preparation of carvedilol and its crystalline hydrate and solvate
IN Hildesheim, Jean; Finogueev, Sergey; Aronhime, Judith; **Dolitzky, Ben-Zion**; Ben-Valid, Shoshana; Kor, Ilan
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2

L8 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Zolpidem hemitartrate polymorphs for treatment of insomnia
IN Aronhime, Judith; **Dolitzky, Ben-Zion**; Kordova, Marco; Leonov, David; Meszaros-Sos, Erzebet; Salyi, Szaboles; Schwartz, Anchel; Szabo, Csaba; Zavurov, Shlomo
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2

L8 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Torsemide polymorphs for edema treatment
IN Aronhime, Judith; Leonov, David; Kordova, Marko; Schwartz, Anchel; **Dolitzky, Ben-Zion**

SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2

L8 ANSWER 42 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
TI Novel synthesis of piperazine ring
IN **Dolitzky, Ben-Zion**
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2

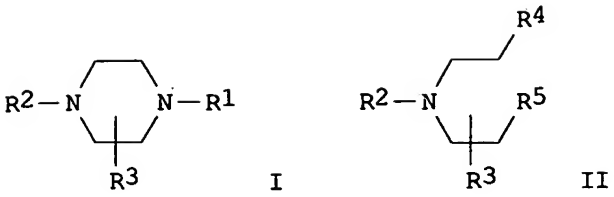
=> d L8 42 ibib abs

L8 ANSWER 42 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:756684 CAPLUS
DOCUMENT NUMBER: 133:321901
TITLE: Novel synthesis of piperazine ring
INVENTOR(S): **Dolitzky, Ben-Zion**
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000063185	A1	20001026	WO 2000-US9418	20000407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2370389	AA	20001026	CA 2000-2370389	20000407
US 6339156	B1	20020115	US 2000-545011	20000407
TR 200103035	T2	20020121	TR 2001-200103035	20000407
EP 1178972	A1	20020213	EP 2000-921933	20000407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002542234	T2	20021210	JP 2000-612277	20000407
AU 777105	B2	20040930	AU 2000-42190	20000407
US 2002035256	A1	20020321	US 2001-939406	20010824
US 6852855	B2	20050208		
ZA 2001008480	A	20021115	ZA 2001-8480	20011016
HR 2001000759	A1	20030228	HR 2001-759	20011018

PRIORITY APPLN. INFO.:	US 1999-130048P	P	19990419
	US 2000-545011	XX	20000407
	WO 2000-US9418	W	20000407

OTHER SOURCE(S): CASREACT 133:321901; MARPAT 133:321901
GI



I II

AB A novel process for preparing the compds I [R1 = (un)subsituted alkyl, alkoxy, aryl, aryloxy, arylalkoxy; R2 = (un)substituted alkyl, alkoxy, aryl, aryloxy, arylalkoxy, tosyl, formyl, acetyl, amino; R3 = (un)substituted alkyl, alkoxy, aryl, aryloxy, arylalkoxy], comprising the step of reacting the compound II [R4, R5 = F, Cl, Br, I] with H2NR1, is disclosed. The compds. I are useful as intermediates in the synthesis of the antidepressant mirtazapine and other tetracyclic compds.

=> d L8 4 ibib abs

L8 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:99457 CAPLUS
DOCUMENT NUMBER: 142:176567
TITLE: Crystallization process for purifying and isolating racemic bicalutamide
INVENTOR(S): **Dolitzky, Ben-Zion**; Reany, Ofer; Shammai, Jenny
PATENT ASSIGNEE(S): Biogal Gyogyszergyar Rt., Hung.; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009946	A1	20050203	WO 2003-US20307	20030625

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2003-US20307 20030625
AB A process for the purification and isolation of bicalutamide by solution crystallization comprises: (i) combining crude bicalutamide and a solvent; (ii) crystallizing the bicalutamide from the solvent; and (iii) collecting the crystals of bicalutamide.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 2-aminobutyramide/cn
REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L26 15 L25

=> d

L26 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:14581 CAPLUS
DN 142:92334
TI Enzymic kinetic resolution of protected amino acids
IN Youshko, Maxim Ilich; Svedas, Vytautas-Juozapas Kajetono; Sheldon, Roger Arthur; Van Langen, Lukas Michael
PA Clea Technologies BV, Neth.; Biotir Ltd.
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005001107	A1	20050106	WO 2004-RU244	20040625

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI NL 2003-1023767 A 20030627
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> exp 2-aminobutyramide

E1	1	1ZZ1R/BI
E2	8326421	2/BI
E3	0	--> 2-AMINOBUTYRAMIDE/BI
E4	2152120	20/BI
E5	12	20-10-0/BI
E6	1	20-10-1/BI
E7	3	20-10-2/BI
E8	3	20-10-3/BI
E9	4	20-10-4/BI
E10	8	20-10-5/BI
E11	3	20-10-6/BI
E12	1	20-10-7/BI

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2.45	249.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL

	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-24.57

FILE 'REGISTRY' ENTERED AT 10:37:47 ON 21 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 20 MAR 2005 HIGHEST RN 845957-95-1
DICTIONARY FILE UPDATES: 20 MAR 2005 HIGHEST RN 845957-95-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

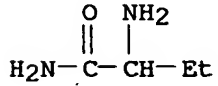
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> s 2-aminobutyramide/cn; d
L27 1 2-AMINOBUTYRAMIDE/CN

L27 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 53726-14-0 REGISTRY
ED Entered STN: 16 Nov 1984
CN Butanamide, 2-amino- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Butyramide, 2-amino- (7CI)
OTHER NAMES:
CN α-Aminobutyramide
CN α-Aminobutyric acid amide
CN **2-Aminobutyramide**
CN DL-2-Aminobutyramide
FS 3D CONCORD
DR 143164-46-9
MF C4 H10 N2 O
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS,
USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

15 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
15 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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=> fil caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         8.16     257.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                         0.00     -24.57

FILE 'CAPLUS' ENTERED AT 10:39:54 ON 21 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 21 Mar 2005  VOL 142 ISS 13
FILE LAST UPDATED: 20 Mar 2005  (20050320/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s 2-amino-butanamide or 2-aminobutyramide or (α-aminobutyramide) or
(α-aminobutyric acid amide)
       8326421 2
       1016591 AMINO
            42 AMINOS
       1016608 AMINO
                  (AMINO OR AMINOS)
           600 BUTANAMIDE
            27 BUTANAMIDES
           616 BUTANAMIDE
                  (BUTANAMIDE OR BUTANAMIDES)
             0 2-AMINO-BUTANAMIDE
                  (2(W)AMINO(W)BUTANAMIDE)
       8326421 2
            80 AMINOBUTYRAMIDE
             6 AMINOBUTYRAMIDES
            85 AMINOBUTYRAMIDE
                  (AMINOBUTYRAMIDE OR AMINOBUTYRAMIDES)
            10 2-AMINOBUTYRAMIDE
                  (2(W)AMINOBUTYRAMIDE)
       1530257 ALPHA
          2487 ALPHAS
       1530357 ALPHA
                  (ALPHA OR ALPHAS)
            80 AMINOBUTYRAMIDE
             6 AMINOBUTYRAMIDES
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            15 A-AMINOBUTYRAMIDE
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      1468913 ACIDS
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       118274 AMIDE
        74887 AMIDES
       161380 AMIDE
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                (ALPHA(W)AMINOBUTYRIC(W)ACID(W)AMIDE)
L28        27 2-AMINO-BUTANAMIDE OR 2-AMINOBUTYRAMIDE OR (A-AMINOBUTYRAM
               IDE) OR (A-AMINOBUTYRIC ACID AMIDE)

=> d L28 ibib abs 1-10

L28  ANSWER 1 OF 27  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:675721  CAPLUS
DOCUMENT NUMBER:          141:174073
TITLE:                    Process for producing levetiracetam
INVENTOR(S):              Dolityzky, Ben-Zion
PATENT ASSIGNEE(S):       Teva Pharmaceutical Industries Ltd., Israel; Teva
                          Pharmaceuticals USA, Inc.; Hildesheim, Jean;
                          Finogueev, Serguei
SOURCE:                   PCT Int. Appl., 17 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2004069796         A2    20040819    WO 2004-US3149           20040203
     WO 2004069796         A3    20050106
         W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
             BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
             CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
             ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
             IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
             LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
             MZ, MZ, NA, NI
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
             MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
     US 2004259933         A1    20041223    US 2004-771821           20040203
PRIORITY APPLN. INFO.:                       US 2003-444550P      P   20030203
                                             US 2003-455795P      P   20030319

OTHER SOURCE(S):          CASREACT 141:174073
AB   Levetiracetam is prepared by reaction of (S)-2-
     aminobutyramide hydrochloride with 4-chlorobutyryl chloride in
     MeCN or Me tert-Bu ether in the presence of a strong base.

L28  ANSWER 2 OF 27  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2003:875255  CAPLUS
DOCUMENT NUMBER:          139:364839
```

TITLE: Preparation of isoquinolines as monoamine oxidase B inhibitors useful against Alzheimer's disease and senile dementia

INVENTOR(S): Cesura, Andrea; Rodriguez Sarmiento, Rosa Maria; Scalone, Michelangelo; Thomas, Andrew William; Wyler, Rene

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091219	A1	20031106	WO 2003-EP3845	20030414
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1501804	A1	20050202	EP 2003-725018	20030414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009562	A	20050215	BR 2003-9562	20030414
US 2003225122	A1	20031204	US 2003-417378	20030416
US 6818774	B2	20041116		

PRIORITY APPLN. INFO.: EP 2002-9253 A 20020426
WO 2003-EP3845 W 20030414

OTHER SOURCE(S): MARPAT 139:364839

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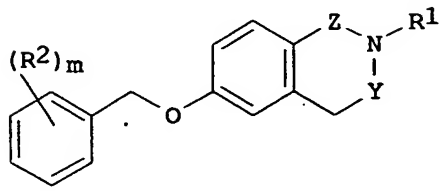


I

AB This invention relates to isoquinolines (shown as I; e.g. 2-[6-(3-fluorobenzyloxy)-1-oxo-3,4-dihydro-1H-isoquinolin-2-yl]acetamide; Y is C:O, or CH2; Z is C:O or CH2; R1 is H or CR3R4R5 (R3 is -(CH2)nC(O)NR6R7, -(CH2)nCOOR8, -CHR9COOR8, -(CH2)nCN, -(CH2)pOR8, -(CH2)nNR6R7, -(CH2)nCF3, -(CH2)nNHC(O)R9, -(CH2)nNHCOOR8, -(CH2)ntetrahydrofuranyl, -(CH2)pSR8, -(CH2)pS(O)R9, or -(CH2)nC(S)NR5R6; R4 is H, C1-C6-alkyl, - (CH2)pOR8, -(CH2)pSR8, or benzyl; R5 is H, C1-C6-alkyl, -(CH2)pOR8, -(CH2)pSR8, or benzyl; R6 and R7 = H or C1-C6-alkyl; R8 is H or C1-C6-alkyl; R9 is C1-C6-alkyl; m = 1-3; n = 0-2; and p = 1-2; R2 = halogen, halogen-(C1-C6)-alkyl, cyano, C1-C6-alkoxy or halogen-(C1-C6)-alkoxy)) as well as to their pharmaceutically acceptable salts. The invention further relates to medicaments containing these compds., a process for their preparation as well as their use for preparation of medicaments

for the treatment or prevention of diseases in which MAO-B inhibitors might be beneficial. IC50 values for 17 examples of I against monoamine oxidase A and B are tabulated, e.g. 0.008 and 0.33 μM for 2-[6-(3-fluorobenzyloxy)-1-oxo-3,4-dihydro-1H-isoquinolin-2-yl]acetamide. Sixty example prepns. of I are included. For example, 6-(3-Fluorobenzyloxy)-3,4-dihydro-2H-isoquinolin-1-one was prepared in 3 steps (49, 65, 87 % yields) starting from 5-methoxy-1-indanone and involving intermediates 6-methoxy-3,4-dihydro-2H-isoquinolin-1-one and 6-hydroxy-3,4-dihydro-2H-isoquinolin-1-one.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:777757 CAPLUS

DOCUMENT NUMBER: 139:292146

TITLE: Preparation of (benzyloxy)phthalimides as inhibitors of monoamine oxidase B

INVENTOR(S): Cesura, Andrea; Rodriguez Sarmiento, Rosa Maria; Thomas, Andrew William; Wyler, Rene

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

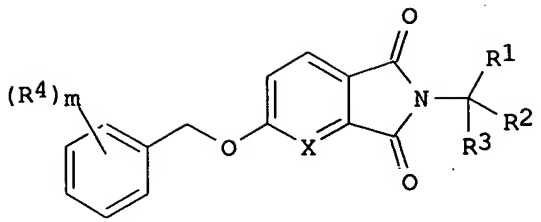
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080573	A1	20031002	WO 2003-EP2931	20030320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003195208	A1	20031016	US 2003-387950	20030313
US 6660736	B2	20031209		
CA 2477771	AA	20031002	CA 2003-2477771	20030320
EP 1490334	A1	20041229	EP 2003-744825	20030320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008786	A	20050111	BR 2003-8786	20030320
US 2004229871	A1	20041118	US 2003-657857	20030909
PRIORITY APPLN. INFO.:			EP 2002-7222	A 20020327
			US 2003-387950	A3 20030313
			WO 2003-EP2931	W 20030320

OTHER SOURCE(S): MARPAT 139:292146

GI



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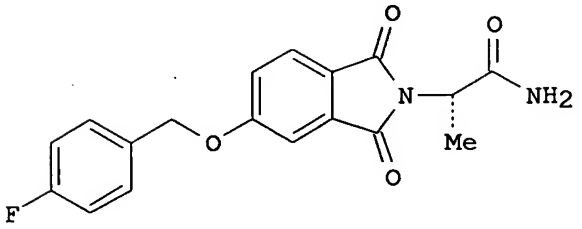

II

AB Title compds. I [wherein X = N or CH; R1 = CONR5R6, CHR7(CH2)nCONR5R6, (CH2)nNR5R6, (CH2)nCO2R8, (CH2)nCN, CHR7(CH2)nCF3, (CH2)nNHCOR9, (CH2)nNHCO2R9, (CH2)pOR8, (CH2)pSR8, (CH2)pSOR9, (CH2)nCSNR5R6, or (un)substituted (CH2)n-piperidinyl, (CH2)n-morpholinyl, (CH2)n-tetrahydrofuranyl, (CH2)n-thiophenyl, (CH2)n-isoxazolyl, (CH2)n-Ph; R2 = H, alkyl, (CH2)pOR10, (CH2)pSR10, or CH2Ph; R3, R5, R6, R8, and R10 = independently H or alkyl; R4 = H, haloalkyl, CN, or (halo)alkoxy; R7 = H, OH, or alkoxy; R9 = alkyl; m = 1-3; n = 0-2; p = 1-2; and pharmaceutically acceptable salts thereof] were prepared as highly selective monoamine oxidase B (MAO-B) inhibitors. For example, reaction of 4-hydroxyphthalic acid with 4-fluorobenzyl bromide in the presence of K2CO3 in acetone and H2O gave 4-(4-fluorobenzyloxy)phthalic acid bis(4-fluorobenzyl)ester (80%). Saponification with LiOH•H2O in THF afforded the acid (56%). Cyclocondensation with alaninamide•HCl using carbonyldiimidazole in 1-methyl-2-pyrrolidinone provided the title isoindole II (49%). The latter preferentially inhibited the enzymic activity of human MAO-B over human MAO-A with IC50 values of 0.008 μM and 0.776 μM, resp. Thus, I and their pharmaceutical compns. are useful for the treatment of diseases mediated by MAO-B, such as Alzheimer's disease and senile dementia (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:851097 CAPLUS
DOCUMENT NUMBER: 135:371992
TITLE: Process for producing optically active α-amino acid and optically active α-amino acid amide by stereoselective microbial hydrolysis of racemic α-amino acid amide
INVENTOR(S): Katoh, Osamu; Uragaki, Toshitaka; Nakamura, Tetsuji
PATENT ASSIGNEE(S): Mitsubishi Rayon Co., Ltd., Japan
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001087819	A1	20011122	WO 2001-JP4191	20010518
W: US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
JP 2001328970	A2	20011127	JP 2000-146663	20000518
JP 2001328971	A2	20011127	JP 2000-150285	20000522
EP 1300392	A1	20030409	EP 2001-930218	20010518
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
US 2003171597	A1	20030911	US 2003-276702	20030414
PRIORITY APPLN. INFO.:			JP 2000-146663 A	20000518
			JP 2000-150285 A	20000522
			WO 2001-JP4191 W	20010518

OTHER SOURCE(S): CASREACT 135:371992; MARPAT 135:371992

AB Described is a process for efficiently producing an optically active α-amino acid and an optically active α-amino acid amide. After contacting with optionally processed bacterial cells capable of hydrolyzing an asym. material in an aqueous medium, the water serving as the solvent is replaced by at least one solvent selected from among linear, branched and cyclic alcs. having 3 or more carbon atoms. From the alc. solution thus obtained, an optically active α-amino acid is preferentially separated out. To the alc. solution containing an optically active α-amino acid amide obtained after separating the optically active α-amino acid, a basic compound (in particular, a potassium compound) is added. Thus, the amide can be purified without being contaminated with the amino acid. The amide is subjected to the racemization step and recycled in the process described above. Thus, 200 g DL-tert-leucinamide was dissolved in a suspension of Enterobacter cloacae N-7901 in distilled water (800 g), stirred at 40° for 52 h, and centrifuged for removing the bacteria to give an aqueous solution containing 10 weight% L-tert-leucine and 10 weight% D-tert-leucinamide (970 g). A portion of this aqueous solution (200 g) was concentrated under reduced pressure to 72 g, mixed with 300 g isopropanol, and concentrated under reduced pressure to give 140 g of a concentrate containing 6.5 weight% H2O which was heated at 1 h, cooled, and then stirred at 15° for 4 h. The precipitated crystals were recovered by suction filtration to give 18.4 g L-tert-leucine containing ≤0.01 weight% D-tert-leucinamide (92% yield).

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:636044 CAPLUS
DOCUMENT NUMBER: 135:195495
TITLE: Preparation of 2-oxo-1-pyrrolidine derivatives and their anticonvulsant activity
INVENTOR(S): Differding, Edmond; Kenda, Benoit; Lallemand, Benedicte; Matagne, Alain; Michel, Philippe; Pasau, Patrick; Talaga, Patrice
PATENT ASSIGNEE(S): UCB, S.A., Belg.
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062726	A2	20010830	WO 2001-EP1992	20010221

WO 2001062726	A3	20020117			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2401033	AA	20010830	CA 2001-2401033		20010221
AU 2001052144	A5	20010903	AU 2001-52144		20010221
EP 1265862	A2	20021218	EP 2001-925354		20010221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001008664	A	20030429	BR 2001-8664		20010221
JP 2003523996	T2	20030812	JP 2001-561734		20010221
NZ 520448	A	20040326	NZ 2001-520448		20010221
EP 1447399	A1	20040818	EP 2004-7733		20010221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
EP 1452524	A1	20040901	EP 2004-7878		20010221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
EP 1477478	A2	20041117	EP 2004-8270		20010221
EP 1477478	A3	20041124			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
ZA 2002005671	A	20031110	ZA 2002-5671		20020716
ZA 2002005837	A	20031104	ZA 2002-5837		20020722
BG 107004	A	20030430	BG 2002-107004		20020814
US 2003120080	A1	20030626	US 2002-204266		20020820
US 6784197	B2	20040831			
NO 2002003997	A	20021022	NO 2002-3997		20020822
US 2004087646	A1	20040506	US 2003-694090		20031028
US 6806287	B2	20041019			
US 2004116507	A1	20040617	US 2003-693917		20031028
PRIORITY APPLN. INFO.:			GB 2000-4297	A	20000223
			EP 2001-925354	A3	20010221
			EP 2001-940256	A3	20010221
			WO 2001-EP1992	W	20010221
			US 2002-204266	A3	20020820

OTHER SOURCE(S): MARPAT 135:195495

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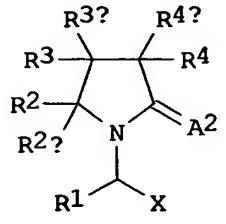

I

AB The title 2-oxo-1-pyrrolidine derivs. I [X = CA1NR5R6, CA1OR7, CA1R8, cyano; A1, A2 = O, S, NR9; R1 = H, alkyl, aryl, CH2R1; R2-R4 = H, halo, OH, SH, etc.; R2a, R3a, R4a = H, halo, alkyl, alkenyl, alkynyl, aryl; R5-R7, R9 = H, OH, alkyl, aryl, heterocyclyl; R8 = H, OH, SH, etc.] were prepared E.g., (2S)-2-[2-oxo-4-(phenoxymethyl)-1-pyrrolidinyl]butanamide was prepared I are particularly suited for treating neurol. disorders such

as epilepsy.

L28 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:552221 CAPLUS
DOCUMENT NUMBER: 131:271840
TITLE: Zeolite-induced heterocyclization: a superior method of synthesis of imidazolidinones
AUTHOR(S): Nooshabadi, Massoud A.; Aghapoor, Kioumars; Bolourtchian, Mohammad; Heravi, Majid M.
CORPORATE SOURCE: Chem. & Chem. Eng. Res. Cent. of Iran, Tehran, Iran
SOURCE: Journal of Chemical Research, Synopses (1999), (8), 498-499
CODEN: JRPSDC; ISSN: 0308-2342
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:271840
AB A superior method for synthesis of imidazolidinones by catalytic action of H-Y zeolite on the reaction of α-amino carboxamides with carbonyl compds. is described.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:546250 CAPLUS
DOCUMENT NUMBER: 129:241632
TITLE: Acyl transfer activity of an amidase from Rhodococcus sp. strain R312: formation of a wide range of hydroxamic acids
AUTHOR(S): Fournand, David; Bigey, Frederic; Arnaud, Alain
CORPORATE SOURCE: Ecole Nationale Superieure Agronomique de Montpellier-Inst. Natl. de la Recherche Agronomique, UFR de Microbiol. Ind. et Genetique des Microorganismes, Montpellier, 34060, Fr.
SOURCE: Applied and Environmental Microbiology (1998), 64(8), 2844-2852
CODEN: AEMIDF; ISSN: 0099-2240
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The enantioselective amidase from Rhodococcus sp. strain R312 was produced in Escherichia coli and was purified in one chromatog. step. This enzyme was shown to catalyze the acyl transfer reaction to hydroxylamine from a wide range of amides. The optimum working pH values were 7 with neutral amides and 8 with α-aminoamides. The reaction occurred according to a Ping Pong Bi Bi mechanism. The kinetic consts. demonstrated that the presence of a hydrophobic moiety in the carbon side chain considerably decreased the Kmamide values (e.g., Kmamide = 0.1 mM for butyramide, isobutyramide, valeramide, pivalamide, hexanoamide, and benzamide). Moreover, very high turnover nos. (kcat) were obtained with linear aliphatic amides (e.g., kcat = 333 s-1 with hexanoamide), whereas branched-side-chain-, aromatic cycle- or heterocycle-containing amides were sterically hindered. Carboxylic acids, α-amino acids, and Me esters were not acyl donors or were very bad acyl donors. Only amides and hydroxamic acids, both of which contained amide bonds, were determined to be efficient acyl donors. On the other hand, the highest affinities of the acyl-enzyme complexes for hydroxylamine were obtained with short, polar or unsatd. amides as acyl donors (e.g., KmNH2OH = 20, 25, and 5 mM for acetyl-, alanyl-, and acryloyl-enzyme complexes, resp.). No acyl acceptors except water and hydroxylamine were found. Finally, the purified amidase was shown to be L-enantioselective towards α-hydroxy- and α-aminoamides.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:157185 CAPLUS
DOCUMENT NUMBER: 120:157185
TITLE: Purification and characterization of an L-aminopeptidase from Pseudomonas putida ATCC 12633
AUTHOR(S): Hermes, H. F. M.; Sonke, T.; Peters, P. J. H.; van Balken, J. A. M.; Kamphuis, J.; Dijkhuizen, L.; Meijer, E. M.
CORPORATE SOURCE: Res. Bio-Organ. Chem. Sect., DSM, Geleen, 6160 MD, Neth.
SOURCE: Applied and Environmental Microbiology (1993), 59(12), 4330-4
CODEN: AEMIDF; ISSN: 0099-2240
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An L-aminopeptidase of Pseudomonas putida, used in an industrial process for the hydrolysis of D,L-amino acid amide racemates, was purified to homogeneity. The highly L-enantioselective enzyme resembled thiol reagent-sensitive alkaline serine proteinases was strongly activated by divalent cations. It possessed a high substrate specificity for dipeptides and α-H amino acid amides, e.g., L-phenylglycine amide.

L28 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:247313 CAPLUS
DOCUMENT NUMBER: 114:247313
TITLE: Preparation of bis(diketopiperazinyl)alkanes as cardioprotectants for use with doxorubicin
INVENTOR(S): Creighton, Andrew Malcolm
PATENT ASSIGNEE(S): National Research Development Corp., UK
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 409499	A2	19910123	EP 1990-307685		19900713
EP 409499	A3	19910327			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
CA 2033203	AA	19910114	CA 1990-2033203		19900713
WO 9100729	A2	19910124	WO 1990-GB1079		19900713
WO 9100729	A3	19910613			
W: AU, CA, JP, US					
AU 9060471	A1	19910206	AU 1990-60471		19900713
GB 2235874	A1	19910320	GB 1990-15437		19900713
JP 04500690	T2	19920206	JP 1990-510521		19900713
ZA 9005511	A	19920325	ZA 1990-5511		19900713
PRIORITY APPLN. INFO.:			GB 1989-16072	A	19890713
			WO 1990-GB1079	A	19900713

OTHER SOURCE(S): MARPAT 114:247313
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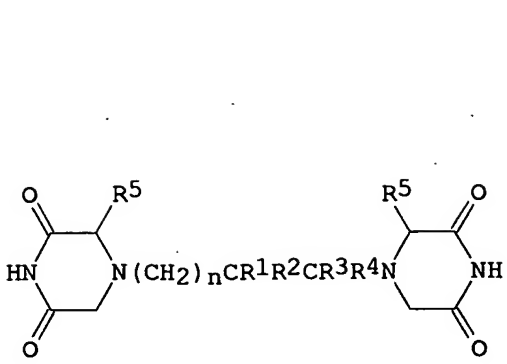

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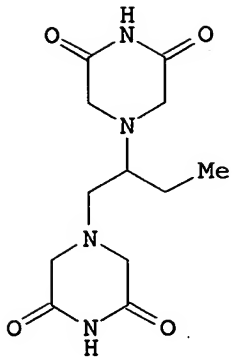

II

AB The title compds. (I; R1-R4 = H, acyclic aliphatic hydrocarbyl, hydroxyalkyl, alkoxyalkyl; or R1, R3 = H; R2R4 = alkylene; R5 = H, acyclic aliphatic hydrocarbyl; n = 0-2) were prepared Thus, a mixture of dl-1,2-diaminobutanetetraacetic acid and HCONH2 were heated under reduced pressure at 100-110° for 1 h and at 155° for 4 h to give 55% title compound II. The latter at 100 mg/kg i.p. in rats dosed with 4 mg/kg i.v. doxorubicin improved cardiac output to 70% of untreated controls, vs. 41% for animals receiving only doxorubicin. Tablets were prepared containing II.

L28 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:5905 CAPLUS
DOCUMENT NUMBER: 112:5905
TITLE: Structure-activity relationships of peptide T-related pentapeptides
AUTHOR(S): Marastoni, M.; Salvadori, S.; Balboni, G.; Spisani, S.; Gavioli, R.; Traniello, S.; Tomatis, R.
CORPORATE SOURCE: Dep. Pharm. Sci., Univ. Ferrara, Ferrara, I-44100, Italy
SOURCE: Arzneimittel-Forschung (1989), 39(8), 926-8
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fifteen pentapeptide analogs of C-terminal fragment of peptide T, H-Ala-Ser-Thr-Thr-Thr-Asn-Tyr-Thr-OH, were prepared and tested for human monocyte chemotaxis. Structure-activity studies suggest that the potent chemotactic activity of H-Thr-Thr-Asn-Tyr-Thr-OH is mediated through the polar properties of the C-terminal carboxyl group and Thr side chains at the critical positions 5 and 8, while the OH group of N-terminal Thr and its free amino function are not essential requirements for CD4 receptor interactions.

=> d L28 ibib abs kwic 1-10

L28 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:675721 CAPLUS
DOCUMENT NUMBER: 141:174073
TITLE: Process for producing levetiracetam
INVENTOR(S): Dolityzky, Ben-Zion
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.; Hildesheim, Jean; Finogueev, Serguei
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004069796	A2	20040819	WO 2004-US3149		20040203
WO 2004069796	A3	20050106			

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004259933	A1	20041223	US 2004-771821		20040203
PRIORITY APPLN. INFO.:			US 2003-444550P	P	20030203
			US 2003-455795P	P	20030319

OTHER SOURCE(S): CASREACT 141:174073

AB Levetiracetam is prepared by reaction of (S)-**2**-**aminobutyramide** hydrochloride with 4-chlorobutyryl chloride in MeCN or Me tert-Bu ether in the presence of a strong base.

AB Levetiracetam is prepared by reaction of (S)-**2**-**aminobutyramide** hydrochloride with 4-chlorobutyryl chloride in MeCN or Me tert-Bu ether in the presence of a strong base.

IT 4635-59-0, 4-Chlorobutyryl chloride 7682-20-4, (S)-**2**-**Aminobutyramide** hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of levetiracetam)

L28 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:875255 CAPLUS
DOCUMENT NUMBER: 139:364839
TITLE: Preparation of isoquinolines as monoamine oxidase B inhibitors useful against Alzheimer's disease and senile dementia
INVENTOR(S): Cesura, Andrea; Rodriguez Sarmiento, Rosa Maria; Scalone, Michelangelo; Thomas, Andrew William; Wyler, Rene
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091219	A1	20031106	WO 2003-EP3845	20030414

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1501804	A1	20050202	EP 2003-725018	20030414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009562	A	20050215	BR 2003-9562	20030414
US 2003225122	A1	20031204	US 2003-417378	20030416
US 6818774	B2	20041116		
PRIORITY APPLN. INFO.:			EP 2002-9253 A	20020426
			WO 2003-EP3845 W	20030414

OTHER SOURCE(S): MARPAT 139:364839

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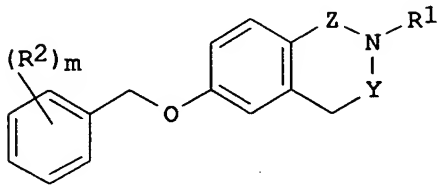

I

AB This invention relates to isoquinolines (shown as I; e.g. 2-[6-(3-fluorobenzyloxy)-1-oxo-3,4-dihydro-1H-isoquinolin-2-yl]acetamide; Y is C:O, or CH2; Z is C:O or CH2; R1 is H or CR3R4R5 (R3 is -(CH2)nC(O)NR6R7, -(CH2)nCOOR8, -CHR9COOR8, -(CH2)nCN, -(CH2)pOR8, -(CH2)nNR6R7, -(CH2)nCF3, -(CH2)nNHC(O)R9, -(CH2)nNHCOOR8, -(CH2)ntetrahydrofuranyl, -(CH2)pSR8, -(CH2)pS(O)R9, or -(CH2)nC(S)NR5R6; R4 is H, C1-C6-alkyl, - (CH2)pOR8, -(CH2)pSR8, or benzyl; R5 is H, C1-C6-alkyl, -(CH2)pOR8, -(CH2)pSR8, or benzyl; R6 and R7 = H or C1-C6-alkyl; R8 is H or C1-C6-alkyl; R9 is C1-C6-alkyl; m = 1-3; n = 0-2; and p = 1-2; R2 = halogen, halogen-(C1-C6)-alkyl, cyano, C1-C6-alkoxy or halogen-(C1-C6)-alkoxy)) as well as to their pharmaceutically acceptable salts. The invention further relates to medicaments containing these compds., a process for their preparation as well as their use for preparation of medicaments for the treatment or prevention of diseases in which MAO-B inhibitors might be beneficial. IC50 values for 17 examples of I against monoamine oxidase A and B are tabulated, e.g. 0.008 and 0.33 μM for 2-[6-(3-fluorobenzyloxy)-1-oxo-3,4-dihydro-1H-isoquinolin-2-yl]acetamide. Sixty example prepns. of I are included. For example, 6-(3-Fluorobenzyloxy)-3,4-dihydro-2H-isoquinolin-1-one was prepared in 3 steps (49, 65, 87 % yields) starting from 5-methoxy-1-indanone and involving intermediates 6-methoxy-3,4-dihydro-2H-isoquinolin-1-one and 6-hydroxy-3,4-dihydro-2H-isoquinolin-1-one.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 105-36-2, Ethyl bromoacetate 406-81-5, 1-Bromo-4,4,4-trifluorobutane 446-48-0, 2-Fluorobenzyl bromide 456-41-7, 3-Fluorobenzyl bromide 459-46-1, 4-Fluorobenzyl bromide 535-11-5, Ethyl 2-bromopropionate 539-74-2, Ethyl 3-bromopropionate 592-55-2, 2-Bromoethyl ethyl ether 621-37-4, 3-Hydroxyphenylacetic acid 766-80-3, 3-Chlorobenzyl bromide 1192-30-9, Tetrahydrofurfuryl bromide 2417-90-5, 3-Bromopropionitrile 3014-80-0 3470-49-3, 5-Hydroxy-1-indanone 5111-70-6, 5-Methoxy-1-indanone 5241-58-7, L-Phenylalanine amide 5875-25-2, 2-Bromopropionamide 6320-96-3, 3-Bromopropionamide 6482-24-2, 2-Bromoethyl methyl ether 7682-20-4, (S)-2-**Aminobutyramide** hydrochloride 10466-61-2 16120-92-6, Methionine amide hydrochloride 23915-07-3, 2,4-Difluorobenzyl bromide 28188-41-2 33208-99-0, L-Alanine amide hydrochloride 65414-74-6, L-Serine amide hydrochloride 71666-94-9, D-Phenylalanine amide

hydrochloride 71810-97-4, D-Alanine amide hydrochloride 85118-00-9, 2,6-Difluorobenzyl bromide 85118-01-0, 3,4-Difluorobenzyl bromide 98190-85-3, Methyl (S)-3-bromo-2-methylpropionate 113211-94-2, 2,3-Difluorobenzyl bromide 122702-20-9, D-Serine amide hydrochloride 141776-91-2, 3,5-Difluorobenzyl bromide 620606-15-7, [6-(4-Fluorobenzyloxy)-1-oxo-3,4-dihydro-1H-isoquinolin-2-yl]acetic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isoquinolines as monoamine oxidase B inhibitors useful against Alzheimer's disease and senile dementia)

L28 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:777757 CAPLUS
DOCUMENT NUMBER: 139:292146
TITLE: Preparation of (benzyloxy)phthalimides as inhibitors of monoamine oxidase B
INVENTOR(S): Cesura, Andrea; Rodriguez Sarmiento, Rosa Maria; Thomas, Andrew William; Wyler, Rene
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080573	A1	20031002	WO 2003-EP2931	20030320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003195208	A1	20031016	US 2003-387950	20030313
US 6660736	B2	20031209		
CA 2477771	AA	20031002	CA 2003-2477771	20030320
EP 1490334	A1	20041229	EP 2003-744825	20030320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008786	A	20050111	BR 2003-8786	20030320
US 2004229871	A1	20041118	US 2003-657857	20030909
PRIORITY APPLN. INFO.:			EP 2002-7222	A 20020327
			US 2003-387950	A3 20030313
			WO 2003-EP2931	W 20030320

OTHER SOURCE(S): MARPAT 139:292146
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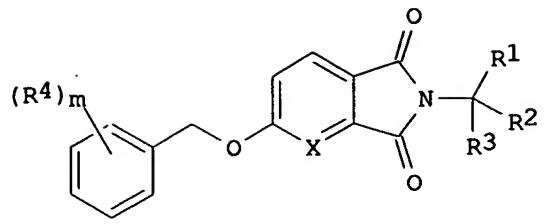

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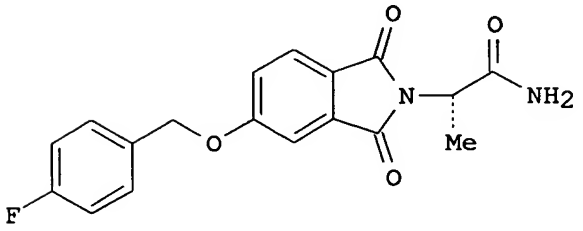

II

AB Title compds. I [wherein X = N or CH; R1 = CONR5R6, CHR7(CH2)nCONR5R6, (CH2)nNR5R6, (CH2)nCO2R8, (CH2)nCN, CHR7(CH2)nCF3, (CH2)nNHCOR9, (CH2)nNHCO2R9, (CH2)pOR8, (CH2)pSR8, (CH2)pSOR9, (CH2)nCSNR5R6, or (un)substituted (CH2)n-piperidinyl, (CH2)n-morpholinyl, (CH2)n-tetrahydrofuranyl, (CH2)n-thiophenyl, (CH2)n-isoxazolyl, (CH2)n-Ph; R2 = H, alkyl, (CH2)pOR10, (CH2)pSR10, or CH2Ph; R3, R5, R6, R8, and R10 = independently H or alkyl; R4 = H, haloalkyl, CN, or (halo)alkoxy; R7 = H, OH, or alkoxy; R9 = alkyl; m = 1-3; n = 0-2; p = 1-2; and pharmaceutically acceptable salts thereof] were prepared as highly selective monoamine oxidase B (MAO-B) inhibitors. For example, reaction of 4-hydroxyphthalic acid with 4-fluorobenzyl bromide in the presence of K2CO3 in acetone and H2O gave 4-(4-fluorobenzyloxy)phthalic acid bis(4-fluorobenzyl)ester (80%). Saponification with LiOH•H2O in THF afforded the acid (56%). Cyclocondensation with alaninamide•HCl using carbonyldiimidazole in 1-methyl-2-pyrrolidinone provided the title isoindole II (49%). The latter preferentially inhibited the enzymic activity of human MAO-B over human MAO-A with IC50 values of 0.008 μM and 0.776 μM, resp. Thus, I and their pharmaceutical compns. are useful for the treatment of diseases mediated by MAO-B, such as Alzheimer's disease and senile dementia (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 109-85-3, 2-Methoxyethylamine 123-00-2, 4-(3-Aminopropyl)morpholine 402-49-3, 4-(Trifluoromethyl)benzyl bromide 431-38-9, 3-Amino-1,1,1-trifluoro-2-propanol 446-48-0, 2-Fluorobenzyl bromide 456-41-7, 3-Fluorobenzyl bromide 459-46-1, 4-Fluorobenzyl bromide 459-56-3, 4-Fluorobenzyl alcohol 589-15-1, 4-Bromobenzyl bromide 610-35-5, 4-Hydroxyphthalic acid 623-33-6, Glycine ethyl ester hydrochloride 874-98-6, 3-Methoxybenzyl bromide 1001-53-2, N-Acetylethylenediamine 1072-67-9, 3-Amino-5-methylisoxazole 2038-03-1, 4-(2-Aminoethyl)morpholine 2050-22-8, Diethyl 2,3-pyridinedicarboxylate 2491-20-5, L-Alanine methyl ester hydrochloride 3014-80-0, L-Valinamide hydrochloride 4795-29-3, Tetrahydrofurfurylamine 5241-58-7, L-Phenylalaninamide 10466-61-2, Leucinamide hydrochloride 13031-62-4, 4-Aminobutyramide hydrochloride 13257-67-5, 2-Methylalanine methyl ester 27578-60-5, 1-(2-Aminoethyl)piperidine 27757-85-3, 2-Thiophenemethylamine 28188-41-2, 3-Bromomethyl benzonitrile 32247-96-4, 3,5-Bis[(trifluoromethyl)benzyl] bromide 33208-99-0, L-Alaninamide hydrochloride 36489-03-9, 2-(Ethylthio)ethylamine 50824-05-0, (4-Trifluoromethoxy)benzyl bromide 51499-72-0, 4-Amino-3-

hydroxybutyramide hydrochloride 52811-68-4, DL-Methioninamide hydrochloride 57260-73-8, tert-Butyl N-(2-aminoethyl)carbamate 63160-13-4, 3-Phenyl-2-(phenylsulfonyl)oxaziridine 65414-74-6, L-Serinamide hydrochloride 71810-97-4, D-Alaninamide hydrochloride 85118-01-0, α-Bromo-3,4-difluorotoluene 87120-72-7, 4-Amino-1-Boc-piperidine 89603-48-5, **2-Aminobutyramide** hydrochloride 99636-32-5, ((S)-1-Methoxypropan-2-yl)amine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (benzyloxy)phthalimide MAO-B selective inhibitor by cyclocondensation of phthalic acids and amino acids or amines for treatment of Alzheimer's disease and dementia)

L28 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:851097 CAPLUS
DOCUMENT NUMBER: 135:371992
TITLE: Process for producing optically active α-amino acid and optically active α-amino acid amide by stereoselective microbial hydrolysis of racemic α-amino acid amide
INVENTOR(S): Katoh, Osamu; Uragaki, Toshitaka; Nakamura, Tetsuji
PATENT ASSIGNEE(S): Mitsubishi Rayon Co., Ltd., Japan
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001087819	A1	20011122	WO 2001-JP4191		20010518
W: US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR					
JP 2001328970	A2	20011127	JP 2000-146663		20000518
JP 2001328971	A2	20011127	JP 2000-150285		20000522
EP 1300392	A1	20030409	EP 2001-930218		20010518
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR					
US 2003171597	A1	20030911	US 2003-276702		20030414
PRIORITY APPLN. INFO.:			JP 2000-146663	A	20000518
			JP 2000-150285	A	20000522
			WO 2001-JP4191	W	20010518

OTHER SOURCE(S): CASREACT 135:371992; MARPAT 135:371992
AB Described is a process for efficiently producing an optically active α-amino acid and an optically active α-amino acid amide. After contacting with optionally processed bacterial cells capable of hydrolyzing an asym. material in an aqueous medium, the water serving as the solvent is replaced by at least one solvent selected from among linear, branched and cyclic alcs. having 3 or more carbon atoms. From the alc. solution thus obtained, an optically active α-amino acid is preferentially separated out. To the alc. solution containing an optically active α-amino acid amide obtained after separating the optically active α-amino acid, a basic compound (in particular, a potassium compound) is added. Thus, the amide can be purified without being contaminated with the amino acid. The amide is subjected to the racemization step and recycled in the process described above. Thus, 200 g DL-tert-leucinamide was dissolved in a suspension of Enterobacter cloacae N-7901 in distilled water (800 g), stirred at 40° for 52 h, and centrifuged for removing the bacteria to give an aqueous solution containing 10 weight% L-tert-leucine and 10 weight% D-tert-leucinamide (970 g). A portion of this aqueous solution (200

g) was concentrated under reduced pressure to 72 g, mixed with 300 g isopropanol, and concentrated under reduced pressure to give 140 g of a concentrate containing 6.5 weight% H2O which was heated at 1 h, cooled, and then stirred at 15° for 4 h. The precipitated crystals were recovered by suction filtration to give 18.4 g L-tert-leucine containing ≤0.01 weight% D-tert-leucinamide (92% yield).

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 5241-59-8P, D-Phenylalaninamide 6485-67-2P, D-Phenylglycinamide 54397-23-8P, D-(p-Hydroxyphenyl)glycinamide 104652-77-9P, D-2-**Aminobutyramide** 319930-78-4P, D-tert-Leucinamide 374629-84-2P, D-(o-Chlorophenyl)glycinamide 374629-86-4P 374629-87-5P, D-(p-Fluorophenyl)glycinamide

RL: BPN (Biosynthetic preparation); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)

(isolation and racemization; preparation of optically active α-amino acid and optically active α-amino acid amide by stereoselective microbial hydrolysis of racemic α-amino acid amide followed by fractional crystallization from aqueous alc.)

IT 700-63-0P, DL-Phenylglycinamide 17193-31-6P, DL-Phenylalaninamide 53726-14-0P, DL-2-**Aminobutyramide** 72151-95-2P, DL-(p-Hydroxyphenyl)glycinamide 113582-42-6P 138228-61-2P, DL-(o-Chlorophenyl)glycinamide 189138-28-1P, DL-(p-Fluorophenyl)glycinamide 374629-85-3P

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

(preparation of optically active α-amino acid and optically active α-amino acid amide by stereoselective microbial hydrolysis of racemic α-amino acid amide followed by fractional crystallization from aqueous alc.)

L28 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:636044 CAPLUS
DOCUMENT NUMBER: 135:195495
TITLE: Preparation of 2-oxo-1-pyrrolidine derivatives and their anticonvulsant activity
INVENTOR(S): Differding, Edmond; Kenda, Benoit; Lallemand, Benedicte; Matagne, Alain; Michel, Philippe; Pasau, Patrick; Talaga, Patrice
PATENT ASSIGNEE(S): UCB, S.A., Belg.
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062726	A2	20010830	WO 2001-EP1992	20010221
WO 2001062726	A3	20020117		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2401033	AA	20010830	CA 2001-2401033		20010221
AU 2001052144	A5	20010903	AU 2001-52144		20010221
EP 1265862	A2	20021218	EP 2001-925354		20010221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001008664	A	20030429	BR 2001-8664		20010221
JP 2003523996	T2	20030812	JP 2001-561734		20010221
NZ 520448	A	20040326	NZ 2001-520448		20010221
EP 1447399	A1	20040818	EP 2004-7733		20010221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
EP 1452524	A1	20040901	EP 2004-7878		20010221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
EP 1477478	A2	20041117	EP 2004-8270		20010221
EP 1477478	A3	20041124			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
ZA 2002005671	A	20031110	ZA 2002-5671		20020716
ZA 2002005837	A	20031104	ZA 2002-5837		20020722
BG 107004	A	20030430	BG 2002-107004		20020814
US 2003120080	A1	20030626	US 2002-204266		20020820
US 6784197	B2	20040831			
NO 2002003997	A	20021022	NO 2002-3997		20020822
US 2004087646	A1	20040506	US 2003-694090		20031028
US 6806287	B2	20041019			
US 2004116507	A1	20040617	US 2003-693917		20031028
PRIORITY APPLN. INFO.:			GB 2000-4297	A	20000223
			EP 2001-925354	A3	20010221
			EP 2001-940256	A3	20010221
			WO 2001-EP1992	W	20010221
			US 2002-204266	A3	20020820

OTHER SOURCE(S): MARPAT 135:195495

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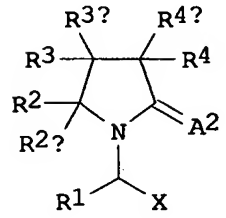


I

AB The title 2-oxo-1-pyrrolidine derivs. I [X = CA1NR5R6, CA1OR7, CA1R8, cyano; A1, A2 = O, S, NR9; R1 = H, alkyl, aryl, CH2R1; R2-R4 = H, halo, OH, SH, etc.; R2a, R3a, R4a = H, halo, alkyl, alkenyl, alkynyl, aryl; R5-R7, R9 = H, OH, alkyl, aryl, heterocyclyl; R8 = H, OH, SH, etc.] were prepared E.g., (2S)-2-[2-oxo-4-(phenoxymethyl)-1-pyrrolidinyl]butanamide was prepared I are particularly suited for treating neurol. disorders such as epilepsy.

IT 96-32-2, Methyl bromoacetate 497-23-4, 2(5H)-Furanone 587-04-2, 3-Chlorobenzaldehyde 617-52-7, Dimethyl itaconate 879-85-6 926-36-3 1099-45-2 3196-15-4, Methyl 2-bromobutanoate 7324-11-0, (S)-**2-Aminobutyramide** 56596-18-0 75190-94-2 78920-10-2 357338-20-6 357338-34-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-oxo-1-pyrrolidine derivs. and their anticonvulsant activity)

L28 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:552221 CAPLUS
DOCUMENT NUMBER: 131:271840
TITLE: Zeolite-induced heterocyclization: a superior method of synthesis of imidazolidinones
AUTHOR(S): Nooshabadi, Massoud A.; Aghapoor, Kioumars; Bolourtchian, Mohammad; Heravi, Majid M.
CORPORATE SOURCE: Chem. & Chem. Eng. Res. Cent. of Iran, Tehran, Iran
SOURCE: Journal of Chemical Research, Synopses (1999), (8), 498-499
CODEN: JRPSDC; ISSN: 0308-2342
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:271840
AB A superior method for synthesis of imidazolidinones by catalytic action of H-Y zeolite on the reaction of α-amino carboxamides with carbonyl compds. is described.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT 67-64-1, 2-Propanone, reactions 78-93-3, 2-Butanone, reactions 98-86-2, Acetophenone, reactions 100-52-7, Benzaldehyde, reactions 108-94-1, Cyclohexanone, reactions 120-92-3, Cyclopentanone 700-63-0 53726-14-0, **2-Aminobutyramide**
RL: RCT (Reactant); RACT (Reactant or reagent)
(zeolite-induced heterocyclization in preparation of imidazolidinones)

L28 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:546250 CAPLUS
DOCUMENT NUMBER: 129:241632
TITLE: Acyl transfer activity of an amidase from Rhodococcus sp. strain R312: formation of a wide range of hydroxamic acids
AUTHOR(S): Fournand, David; Bigey, Frederic; Arnaud, Alain
CORPORATE SOURCE: Ecole Nationale Superieure Agronomique de Montpellier-Inst. Natl. de la Recherche Agronomique, UFR de Microbiol. Ind. et Genetique des Microorganismes, Montpellier, 34060, Fr.
SOURCE: Applied and Environmental Microbiology (1998), 64(8), 2844-2852
CODEN: AEMIDF; ISSN: 0099-2240
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The enantioselective amidase from Rhodococcus sp. strain R312 was produced in Escherichia coli and was purified in one chromatog. step. This enzyme was shown to catalyze the acyl transfer reaction to hydroxylamine from a wide range of amides. The optimum working pH values were 7 with neutral amides and 8 with α-aminoamides. The reaction occurred according to a Ping Pong Bi Bi mechanism. The kinetic consts. demonstrated that the presence of a hydrophobic moiety in the carbon side chain considerably decreased the Kmamide values (e.g., Kmamide = 0.1 mM for butyramide, isobutyramide, valeramide, pivalamide, hexanoamide, and benzamide). Moreover, very high turnover nos. (kcat) were obtained with linear aliphatic amides (e.g., kcat = 333 s-1 with hexanoamide), whereas branched-side-chain-, aromatic cycle- or heterocycle-containing amides were sterically hindered. Carboxylic acids, α-amino acids, and Me esters were not acyl donors or were very bad acyl donors. Only amides and hydroxamic acids, both of which contained amide bonds, were determined to be efficient acyl donors. On the other hand, the highest affinities of the acyl-enzyme complexes for hydroxylamine were obtained with short, polar or unsatd. amides as acyl donors (e.g., KmNH2OH = 20, 25, and 5 mM for acetyl-, alanyl-, and acryloyl-enzyme complexes, resp.). No acyl

acceptors except water and hydroxylamine were found. Finally, the purified amidase was shown to be L-enantioselective towards α-hydroxy- and α-aminoamides.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 55-21-0, Benzamide 56-85-9, L-Glutamine, biological studies 57-13-6, Urea, biological studies 60-35-5, Acetamide, biological studies 70-47-3, L-Asparagine, biological studies 75-12-7, Formamide, biological studies 79-05-0, Propionamide 79-06-1, Acrylamide, biological studies 79-39-0, Methacrylamide 98-92-0, Nicotinamide 108-13-4, Malonamide 110-14-5, Succinamide 541-35-5, Butyramide 563-83-7, Isobutyramide 598-41-4, Glycinamide 598-81-2 625-77-4, Diacetamide 626-97-1, Valeramide 628-02-4, Hexanamide 628-94-4, Adipamide 687-51-4, L-Leucinamide 700-63-0, DL-Phenylglycinamide 754-10-9, Pivalamide 1453-82-3, Isonicotinamide 2043-43-8, DL-Lactamide 4510-08-1, L-Methioninamide 4540-60-7, L-Valinamide 4726-85-6, β-Alaninamide 5241-58-7, L-Phenylalaninamide 6791-49-7, L-Serinamide 7324-05-2, L-Alaninamide 7531-52-4, L-Prolinamide 17193-31-6, DL-Phenylalaninamide 19298-72-7, DL-Methioninamide 20696-57-5, L-Tryptophanamide 35320-22-0, D-Alaninamide 49705-99-9, L-Threonineamide 53726-14-0, α -**Aminobutyramide** 89673-71-2 128385-41-1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(acyl transfer activity of amidase from Rhodococcus sp. strain R312: formation of a wide range of hydroxamic acids)

L28 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:157185 CAPLUS
DOCUMENT NUMBER: 120:157185
TITLE: Purification and characterization of an L-aminopeptidase from Pseudomonas putida ATCC 12633
AUTHOR(S): Hermes, H. F. M.; Sonke, T.; Peters, P. J. H.; van Balken, J. A. M.; Kamphuis, J.; Dijkhuizen, L.; Meijer, E. M.
CORPORATE SOURCE: Res. Bio-Organ. Chem. Sect., DSM, Geleen, 6160 MD, Neth.
SOURCE: Applied and Environmental Microbiology (1993), 59(12), 4330-4
CODEN: AEMIDF; ISSN: 0099-2240
DOCUMENT TYPE: Journal
LANGUAGE: English

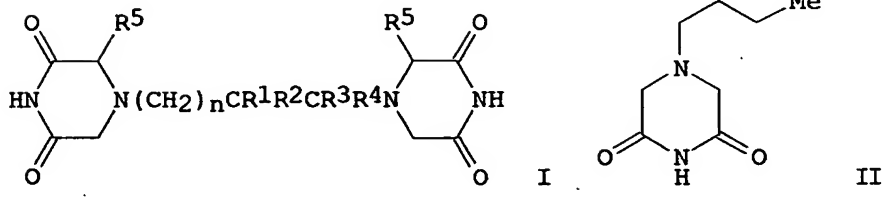
AB An L-aminopeptidase of Pseudomonas putida, used in an industrial process for the hydrolysis of D,L-amino acid amide racemates, was purified to homogeneity. The highly L-enantioselective enzyme resembled thiol reagent-sensitive alkaline serine proteinases was strongly activated by divalent cations. It possessed a high substrate specificity for dipeptides and α-H amino acid amides, e.g., L-phenylglycine amide.

IT 60-35-5, Acetamide, biological studies 79-05-0, Propionamide 79-06-1, Acrylamide, biological studies 79-39-0, Methacrylamide 98-92-0, Nicotinamide 541-35-5, Butyramide 563-83-7, Isobutyramide 598-41-4, Glycine amide 636-65-7 640-19-7, Fluoroacetamide 687-51-4, L-Leucine amide 754-10-9, Pivalamide 2812-47-7, DL-Pproline amide 4410-31-5, DL-Mandelic acid amide 4510-08-1, L-Methionine amide 4540-60-7, L-Valine amide 5241-58-7, L-Phenylalanine amide 6485-52-5, L-Phenylglycine amide 6791-49-7, L-Serine amide 7324-05-2, L-Alanine amide 7324-11-0, L-α -**Aminobutyramide** 14445-54-6, L-Isoleucine amide 20696-57-5, L-Tryptophan amide 40963-14-2
RL: BIOL (Biological study)
(aminopeptidase of Pseudomonas putida substrate specificity for, structure in relation to)

L28 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:247313 CAPLUS
DOCUMENT NUMBER: 114:247313
TITLE: Preparation of bis(diketopiperazinyl)alkanes as cardioprotectants for use with doxorubicin
INVENTOR(S): Creighton, Andrew Malcolm
PATENT ASSIGNEE(S): National Research Development Corp., UK
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 409499	A2	19910123	EP 1990-307685		19900713
EP 409499	A3	19910327			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
CA 2033203	AA	19910114	CA 1990-2033203		19900713
WO 9100729	A2	19910124	WO 1990-GB1079		19900713
WO 9100729	A3	19910613			
W: AU, CA, JP, US					
AU 9060471	A1	19910206	AU 1990-60471		19900713
GB 2235874	A1	19910320	GB 1990-15437		19900713
JP 04500690	T2	19920206	JP 1990-510521		19900713
ZA 9005511	A	19920325	ZA 1990-5511		19900713
PRIORITY APPLN. INFO.:			GB 1989-16072	A	19890713
			WO 1990-GB1079	A	19900713

OTHER SOURCE(S): MARPAT 114:247313
GI



AB The title compds. (I; R1-R4 = H, acyclic aliphatic hydrocarbyl, hydroxyalkyl, alkoxyalkyl; or R1, R3 = H; R2R4 = alkylene; R5 = H, acyclic aliphatic hydrocarbyl; n = 0-2) were prepared Thus, a mixture of dl-1,2-diaminobutanetetraacetic acid and HCONH2 were heated under reduced pressure at 100-110° for 1 h and at 155° for 4 h to give 55% title compound II. The latter at 100 mg/kg i.p. in rats dosed with 4 mg/kg i.v. doxorubicin improved cardiac output to 70% of untreated controls, vs. 41% for animals receiving only doxorubicin. Tablets were prepared containing II.

IT 7324-11-0P, S-2-**Aminobutyramide**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reduction of)

L28 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:5905 CAPLUS
DOCUMENT NUMBER: 112:5905
TITLE: Structure-activity relationships of peptide T-related pentapeptides
AUTHOR(S): Marastoni, M.; Salvadori, S.; Balboni, G.; Spisani, S.; Gavioli, R.; Traniello, S.; Tomatis, R.
CORPORATE SOURCE: Dep. Pharm. Sci., Univ. Ferrara, Ferrara, I-44100, Italy
SOURCE: Arzneimittel-Forschung (1989), 39(8), 926-8
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fifteen pentapeptide analogs of C-terminal fragment of peptide T, H-Ala-Ser-Thr-Thr-Thr-Asn-Tyr-Thr-OH, were prepared and tested for human monocyte chemotaxis. Structure-activity studies suggest that the potent chemotactic activity of H-Thr-Thr-Asn-Tyr-Thr-OH is mediated through the polar properties of the C-terminal carboxyl group and Thr side chains at the critical positions 5 and 8, while the OH group of N-terminal Thr and its free amino function are not essential requirements for CD4 receptor interactions.
IT 72-19-5, Threonine, reactions 2483-62-7, Methyl α-aminobutyrate 2835-81-6, α-Aminobutyric acid 3373-59-9, Threonine methyl ester 25991-17-7, Threoninamide 53726-14-0, α - **Aminobutyramide**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tyrosine derivative)

=> d L28 ibib abs kwic 11-27

L28 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:569822 CAPLUS
DOCUMENT NUMBER: 111:169822
TITLE: Properties of a novel D-stereospecific aminopeptidase from Ochrobactrum anthropi
AUTHOR(S): Asano, Yasuhisa; Nakazawa, Akiko; Kato, Yasuo; Kondo, Kiyosi
CORPORATE SOURCE: Sagami Chem. Res. Cent., Sagamihara, 229, Japan
SOURCE: Journal of Biological Chemistry (1989), 264(24), 14233-9
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel aminopeptidase active toward D-amino acid-containing peptides, D-amino acid amides, and D-amino acid esters was purified 2800-fold to homogeneity from a bacterium O. anthropi SCRC C1-38, which was isolated from soil. The enzyme has a mol. weight of about 122,000 and is composed of 2 identical subunits (Mr = 59,000). The optimal pH for activity was 8.0. It showed strict D-stereospecificity toward substrates including low-mol.-weight D-amino acid amides such as D-alanine amide, D-α - **aminobutyric acid amide**, and D-serine amide; D-alanine N-alkylamides such as D-alanine-p-nitroanilide, D-alanine benzylamide, and D-alanine n-butylamide; and peptides with a D-alanine at the N-terminus such as D-alanylglycine, D-alanylglycylglycine, D-alanyl-L-alanyl-L-alanine, and D-alanine oligomers. Generally, the enzyme did not act on substrates composed of L-amino acid at the N-terminus, although it showed low stereospecificity only toward substrates such as the Me esters of L-alanine, L-serine, and L-alanine-p-nitroanilide. Comparing the Km and Vmax values for the major substrates, it is clear that the enzyme prefers peptides to amino acid

arylamides or amino acid amides. The enzyme was tentatively named as D-aminopeptidase. The enzyme appears to be a thiol peptidase.

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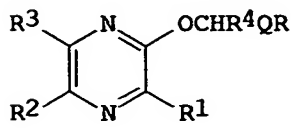
L28 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:23912 CAPLUS
DOCUMENT NUMBER: 110:23912
TITLE: Preparation of 2-substituted alkoxy-3-substituted-pyrazines useful as pharmaceuticals for treating circulatory and metabolic disorders
INVENTOR(S): Yaso, Masao; Suzuki, Yukio; Shibata, Kensuke; Mochizuki, Daisuke; Hayashi, Eiichi
PATENT ASSIGNEE(S): Toyo Jozo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 86 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 252670	A2	19880113	EP 1987-305796		19870630
EP 252670	A3	19890111			
EP 252670	B1	19920115			
R: DE, ES, FR, IT					
JP 63107968	A2	19880512	JP 1987-155394		19870624
US 4894453	A	19900116	US 1987-68228		19870630
ES 2038180	T3	19930716	ES 1987-305796		19870630
US 5001237	A	19910319	US 1989-381958		19890719
PRIORITY APPLN. INFO.:			JP 1986-153742	A	19860630
			JP 1986-153743	A	19860630
			US 1987-68228	A3	19870630

OTHER SOURCE(S): CASREACT 110:23912; MARPAT 110:23912
GI



I

AB Title compds. I [Q = CO, CH2; R = HO, C1-4 alkoxy, halo, C1-4

hydroxyalkyleneamino, C1-4 haloalkyleneamino, di-C1-4 alkylamino, cyclic amino, morpholino, arylpyrazinyl, etc.; R1 = alkyl, aryl-C1-4 alkyl;R2, R3 = C1-4 aryl, R2R3 = (CH2)4; R4 = H, C1-4 alkyl, (un)substituted Ph] or a pharmaceutically acceptable salt thereof, were prepared I [R = HO; R1 = C5H11; R2R3 = (CH2)4; Q = CH2; R4 = H] was chlorinated with SOCl2, treated with aqueous K2CO3, extracted with CHCl3, and to the extract added C6H6, Et3N and
N-butylpiperazine to give I [R = N-butylpiperazino; R1 = C5H11; R2R3 = (CH2)4; R4 = H; Q = CH2] (II) in 52.1% yield. II.HCl at 100 μM showed 97% inhibition of platelet aggregation induced by platelet activation factor.

IT 56-41-7, Alanine, reactions 1187-54-8 10466-60-1 13880-18-7 13880-19-8 13880-20-1 13880-22-3 13880-24-5 13880-26-7 51703-58-3, α-Amino-2-phenylacetamide hydrochloride 53726-14-0, α -**Aminobutyramide** 65864-22-4, Phenylalaninamide hydrochloride 93029-42-6 93169-29-0 118158-39-7 118158-54-6 118158-55-7 118158-56-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with cyclohexanedione)

L28 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:149163 CAPLUS
DOCUMENT NUMBER: 108:149163
TITLE: Preparation of an aqueous solution of an alkali metal salt of methionine for animal feed additives
INVENTOR(S): Gillonnier, Claude; Moisson, Rene
PATENT ASSIGNEE(S): A.E.C. Societe de Chimie Organique et Biologique, Fr.
SOURCE: Fr. Demande, 9 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2590896	A1	19870605	FR 1985-17847	19851203
FR 2590896	B1	19880722		
JP 62132853	A2	19870616	JP 1986-286124	19861202
JP 07008852	B4	19950201		
EP 228938	A1	19870715	EP 1986-402667	19861202
EP 228938	B1	19890308		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
AT 41148	E	19890315	AT 1986-402667	19861202
CA 1261348	A1	19890926	CA 1986-524332	19861202
SU 1598867	A3	19901007	SU 1986-4028573	19861202
US 4960932	A	19901002	US 1988-251854	19881003
US 5147664	A	19920915	US 1991-807664	19911216

PRIORITY APPLN. INFO.:

FR 1985-17847	A	19851203
US 1986-936393	B1	19861201
EP 1986-402667	A	19861202
US 1988-251846	B1	19881003
US 1990-545757	B1	19900629

AB 4-Methylmercapto-**2-aminobutyramide**, at 30-60%, preferably 40-55%, is heated in an autoclave at 100-200° for 5-10 min with 1-1.1 mol alkali metal hydroxide, preferably Na, per mol amide; NH3 is removed; and the solution is cooled to give a solution directly useable as an additive for feed. The above amide 0.60 mol was treated with caustic soda 0.63 mol. in water at 120° for 20 min, NH3 was removed under reduced pressure, and the solution was cooled to 20°. Na methioninate was obtained in 99% yield and used as an additive in chicken feed.

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L28 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:571123 CAPLUS
DOCUMENT NUMBER: 101:171123
TITLE: 2,3-Quinolinedicarboxylic acids
INVENTOR(S): Ladner, David W.
PATENT ASSIGNEE(S): American Cyanamid Co. , USA
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4459409	A	19840710	US 1982-381827	19820525
PRIORITY APPLN. INFO.:			US 1982-381827	19820525

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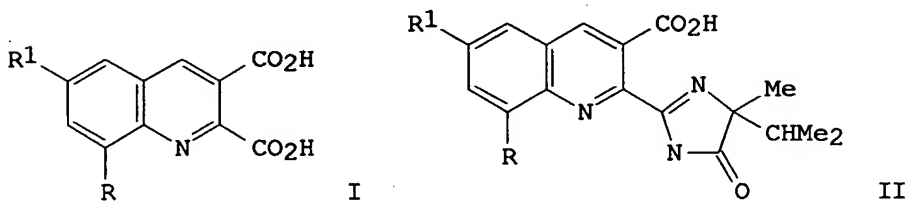

I II

AB Diacids I (one of R and R1 is H and the other is H, CF3, NO2, OCHF2) were prepared from methylquinolinecarboxylic acids, and I were converted to imidazolinyl-substituted quinolines II, which exhibited herbicidal activity. 2-Methyl-3-quinolinecarboxylic acid was treated with Ni peroxide in NaOH to give I (R = R1 = H), the latter was selectively amidated by Me2CHC(NH2)MeCONH2, and the amide was heated with NaOH at 75-80° to give II (R = R1 = H).

IT 4945-42-0P 90376-75-3P 92513-59-2P 92513-60-5P 92513-62-7P 92513-63-8P 92513-64-9P 92513-65-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and ring cleavage of, by α -**aminobutyramide** derivative)

IT 92513-54-7P 92513-55-8P 92513-56-9P 92513-57-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and ring cleavage of, by α -**aminobutyramide** derivs.)

IT 92513-49-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and selective amidation of, by α -**aminobutyramide** derivs.)

L28 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1979:161872 CAPLUS
DOCUMENT NUMBER: 90:161872
TITLE: The identification of eight hydroxylated metabolites of etidocaine by chemical ionization mass spectrometry
AUTHOR(S): Vine, J.; Morgan, D.; Thomas, J.
CORPORATE SOURCE: Dep. Pharm., Univ. Sydney, Sydney, Australia
SOURCE: Xenobiotica (1978), 8(8), 509-13
CODEN: XENOBH; ISSN: 0049-8254
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Following administration of etidocaine-HCl [36637-19-1] (200 mg, orally) to man, 8 hydroxylated metabolites found in urine were extracted out at pH 9.5 and identified as N-(2,6-dimethyl-3-hydroxyphenyl)- [69754-73-0] and N-(2,6-dimethyl-4-hydroxyphenyl)-**2-aminobutyramide** [69754-69-4], N-(2,6-dimethyl-4-hydroxyphenyl)- [69754-74-1] and N-(2,6-dimethyl-3-hydroxyphenyl)-2-(N-ethylamino)butyramide [69754-70-7], N-(2,6-dimethyl-3-hydroxyphenyl)- [69754-75-2] and N-(2,6-dimethyl-4-hydroxyphenyl)-2-(N-propylamino)butyramide [69754-71-8], and N-(2,6-dimethyl-3-hydroxyphenyl)- [69754-76-3] and N-(2,6-dimethyl-4-hydroxyphenyl)-2-(N,N-ethylpropylamino)butyramide [69754-72-9]. These 8 metabolites represented .apprx.10% of the dose administered.

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L28 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1974:532189 CAPLUS
DOCUMENT NUMBER: 81:132189
TITLE: Role of carboxyl, imidazole, and amino groups in inorganic pyrophosphatase of baker's yeast
AUTHOR(S): Heitmann, P.; Uhlig, H. J.
CORPORATE SOURCE: Inst. Physiol. Biol. Chem., Humboldt-Univ. Berlin, Berlin, Ger. Dem. Rep.
SOURCE: Acta Biologica et Medica Germanica (1974), 32(6), 565-74
CODEN: ABMGAJ; ISSN: 0001-5318
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The carboxyl, imidazole, and amino groups of yeast inorg. pyrophosphatase (I) were modified by treatment of the enzyme with H2O-soluble carbodiimides, Et chloroformate, and trinitrobenzenesulfonate, resp. The carbodiimides effected total loss of enzymic activity, which could not be restored by addition of NH2OH. Expts. in the presence of the nucleophile .**alpha**.-**aminobutyramide** indicated that the modification of a relatively small number of carboxyl groups is sufficient to cause strong inactivation. The Ca pyrophosphate complex protected the enzyme effectively against inactivation by carbodiimides. Therefore, ≥1 carboxyl group plays an important role in the mechanism of I, probably by direct interaction with the substrate. The chemical modification of all the amino or imidazole groups was accompanied only by partial enzyme inactivation which indicates that these groups are not essential for the action of the enzyme. The enzyme was completely inactivated by treatment with phenylglyoxal. Ca pyrophosphate exhibited a strong protective effect. Thus, arginine plays an important role in the mechanism of the

enzyme.

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L28 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1966:44161 CAPLUS
DOCUMENT NUMBER: 64:44161
ORIGINAL REFERENCE NO.: 64:8294b-d
TITLE: Condensation of vinyl ethers with amides of amino acids
AUTHOR(S): Adomaitiene, S.; Sladkova, A. M.
SOURCE: Lietuvos TSR Aukstuju Mokyklu Mokslo Darbai, Chem. ir Chem. Technol. (1965), 6, 77-80
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB By the reaction of amides of alanine, nicotinic, and p-aminobenzoic acids with vinyl ethyl ether and vinyl butyl ether (a few drops of concentrated HCl was used as catalyst) at a high temperature, undefined products were obtained. When amides of N-carbobenzoxyamino acids were used, the reaction afforded crystalline products. The reactions were carried out by heating 1 mole ether with 1 mole amide in acetone in the presence of concentrated HCl. The heating was stopped when solution occurred. During 12-14 hrs. the product crystallized When the reaction time was increased, resinous products were formed. Extremely sensitive to the high temperature and longer reaction time were amides of carbobenzoxymethionine and carbobenzoxyproline. The following compds. were prepared (% yield and m.p. given): ethylidenebis(O-carbobenzoxy)glycinamide, 95,178-9° (absolute ethanol); ethylidene (O-carbobenzoxy)-α-alaninamide, 95, 219-20° (absolute ethanol); ethylidenebis(O-carbobenzoxy)-β-alaninamide, 85, 215-16°; ethylidenebis(Ocarbobenzoxy)-α **-aminobutyramide**, 95, 229-30°; ethylidenebis(Ocarbobenzoxy)leucinamide, 85, 196-7°, ethylidenebis(O-carbobenzoxy)-1-valinamide, 85, 236-7°; ethylidenebis(O-carbobenzoxy)methioninamide, 85, 166-7°; ethylidenebis(O-carbobenzoxy)prolinamide, 85, 206-7°; ethylidenebis(O-carbobenzoxy)-β-phenyl-β-alaninamide, 85, 212-13°.

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L28 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1964:448151 CAPLUS
DOCUMENT NUMBER: 61:48151
ORIGINAL REFERENCE NO.: 61:8397e-h,8398a-h,8399a-h,8400a-h,8401a-h,8402a
TITLE: Syntheses of structural analogs of eledoisin. III
AUTHOR(S): Sandrin, Ed.; Boissonnas, R. A.
CORPORATE SOURCE: Sandoz S.A., Basel, Switz.
SOURCE: Helvetica Chimica Acta (1964), 47(5), 1294-1132
CODEN: HCACAV; ISSN: 0018-019X
DOCUMENT TYPE: Journal
LANGUAGE: French

AB The synthesis, and biol. properties of a large number of eledoisin analogs, some of which possess a more potent depressor effect than the original peptide, are described. Whereas the C-terminal moiety of the eledoisin mol. seems to be responsible for its biol. action, its terminal moiety can be deeply modified, or even left out without considerable decrease of activity. There is apparently no relation between the isoelec. points of these peptides and their biol. properties. (Abbreviations used in this article: CBO = benzyloxycarbonyl; CTB = tert-butoxycarbonyl; OBN = p-nitrobenzyloxy; Nor = norvaline; Pyr = pyroglutamic acid; Nle = norleucine; But = α-aminobutyric acid). Condensation of N-CTB-L-Pro-L-Ser-NHNH2 (I) with Nε-CBO-L-Lys-OMe by the azide method gave 51% N-CTB-Pro-Ser-Nε-CBO-Lys-OMe (II), m. 45-50°; [α]22D -54° ± 1° (c 2, 95% AcOH), -34° ± 1° (c 2, HCONMe2), -50.5° ± 1° (c 2, MeOH). Condensation of I with N-CTB-L-Pro-L-Ser-L-Lys-OMe (obtained from the hydrogenation of II) by the azide method gave 65% N-CTB-L-Pro-L-Ser-Nε-(N-CTB-L-Pro-L-Ser)-L-Lys-OMe (III), m. 98°; [α]22D -73° ± 1° (c 2, 95% AcOH), -48° ± 1° (c 2, HCONM2), -66° ± 1° (c 2, MeOH). The reaction of III with N2H4.H2O gave N-CTB-L-Pro-L-Ser-Nε-(N-CTB-L-Pro-L-Ser)-L-Lys-NHNH2 (IV), m. 135°; [α]22D -76° ± 1° (c 2, 95% AcOH), -42.5° ± 1° (c 2, HCONMe2), -68.5° ± 1°(c 2, MeOH). Condensation of N-benzyl-L-Pyr with N-benzyl-L-Pyr-L-Pro-L-Lys-OMe by the dicyclohexylcarbodiimide method gave 70% N-benzyl-L-Pyr-L-Pro-Nε-(N-benzyl-L-Pyr)-L-Lys-OMe (V), m. 90° (decomposition); [α]22D -25.5° ± 1° (c 2, 95% AcOH), -20° ± 1° (c 2, HCONMe2), -31° ± 1° (c 2, MeOH). The reaction of V with N2H4.H2O gave 69% N-benzyl-L-Pyr-L-Pro-Nε-(N-benzyl-L-Pyr)-L-Lys-NHNH2 (VI), m. 105° (decomposition); [α]22D -42° ± 1° (c 2, 95% AcOH), -28.5° ± 1° (c 2, HCONMe2), -41.5° ± 1° (c 2, MeOH). Condensation of N-CTB-L-Asp-L-Ala-L-Phe-L-Ilev-NHNH2 (VII) with Gly-L-Leu-L-But-NH2 by the azide method gave 50% N-CTB-L-Asp-L-Ala-L-Phe-L-Ilev-Gly-L-Leu-L-But-NH2 (VIII), m. 250° (decomposition); [α]22D -45.5° ± 1° (c 1, 95%, AcOH), -31° ± 1° (c 1, HCONMe2). The reaction of VIII with CF3CO2H gave 95% L-Asp-L-Ala-L-Phe-L-Ilev-Gly-L-Leu-L-But-NH2.CF3CO2H, m. 260° (decomposition); [α]22D -33° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Asp(NH2)-L-Ala-L-Phe-L-Ilev-NHNH2 with Gly-L-Leu-L-Met-NH2.HOAc (IX) by the azide method gave 78%

N-CTB-L-Asp(NH2)-L-Ala-L-Phe-L-Ilev-Gly-L-Leu-L-Met-NH2 (X), m. 260° (decomposition); [α]22D -38° ± 1° (c 1, 95% AcOH), -34.5° ± 1° (c 1, HCONMe2). Condensation of N-CTB-L-Asp(NH2)-L-Ala-L-Phe-NHNH2 with L-Ilev-Gly-L-Leu-L-Met-NH2 (XI) by the azide method gave also 33% X. The reaction of X with CF3CO2H gave 100% L-Asp(NH2)-L-Ala-L-Phe-L-Ilev-Gly-L-Leu-L-Met-NH2.CF3CO2H (XII), m. 252° (decomposition); [α]22D -31° ± 1° (c 1, 95% AcOH). The reaction of XII with N NaOH gave 78% L-Asp(NH2)-L-Ala-L-Phe-L-Ilev-Gly-L-Leu-L-Met-NH2, m. 230° (decomposition). Condensation of VII with IX by the azide method gave 62-5% N-CTB-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (XIII), m. 250° (decomposition); [α]22D -34.5° ± 1° (c 2, HCONMe2). The reaction of XIII with CF3CO2H gave 100% L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H (XIV), m. .apprx. 250° (decomposition); [α]22D -21.5° ± 1° (c 0.9, HCONMe2). Condensation of VII with Gly-L-Leu-L-Met by the azide method gave 27% N-CTB-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met (XV), m. 190° (decomposition); [α]22D -33.5° ± 1° (c 1, 95% AcOH), -32° ± 1° (c 1, HCONMe2). The reaction of XV with CF3CO2H gave 90% L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met.CF3CO2H, m. 250° (decomposition); [α]22D -30° ± 1° (c 1, 95% AcOH). Condensation of VII with Gly-L-Leu-L-Met-NH2 sulfoxide by the azide method gave 17% N-CTB-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 sulfoxide (XVI), m. 250° (decomposition); [α]22D -31° ± 1° (c 1, 95% AcOH), -18.5° ± 1° (c 1, HCONMe2). The reaction of XVI with CF3CO2H gave 95% L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 sulfoxide CF3CO2H, m. 240° (decomposition); [α]22D -21.5° ± 1° (c 1, 95% AcOH). Condensation of VII with Gly-L-Leu-L-Nle-NH2 by the azide method gave 55% N-CTB-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Nle-NH2 (XVII), m. 255° (decomposition); [α]22D -40° ± 1° (c 1,95% AcOH), -31° ± 1° (c 1, HCONMe2). The reaction of XVII with CF3CO2H gave 95% L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Nle-NH2.CF3CO2H, m. 260° (decomposition); [α]22D -33.5° ± 1° (c 1, 95% AcOH). Condensation of VII with Gly-L-Leu-L-Nor-NH2 by the azide method gave 59% N-CTB-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Nor-NH2 (XVIII), m. 255° (decomposition); [α]22D -43° ± 1° (c 1, 95% AcOH), -29.5° ± 1° (c 1, HCONMe2). The reaction of VIII with CF3CO2H gave 95% L-Asp-L-Ala-L-Phe-L-Ilev-Gly-L-Leu-L-Nor-NH2.CF3CO2H, m. 260° (decomposition); [α]22D -32° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Pro-L-Ser-Nε-CTB-L-Lys-NHNH2 (XIX) with XI by the azide method gave 52% N-CTB-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Ileu-Gly-L-Leu-L-Met-NH2 (XX), m. 260° (decomposition); [α]22D -56.5° ± 1° (c 1, 95% AcOH). The reaction of XX with CF3CO2H gave 90% L-Pro-L-Ser-L-Lys-L-Ileu-Gly-L-Leu-L-Met-NH2.2CF3CO2H, m. 150° (decomposition); [α]22D -44° ± 1° (c 1, 95% AcOH). Condensation of N-benzyl-L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-NHNH2 (XXI) with Me L-Asp (NH2)-L-Ala-L-Phe (XXII) by the azide method gave 22% Me N-benzyl-L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp(NH2)-L-Ala-L-Phe (XXIII), m. 160° (decomposition); [α]22D -54° ± 1° (c 1, 95% AcOH), -48° ± 1° (c 1, HCONMe2). The reaction of XXIII with N2H4.H2O gave 67% N-benzyl-L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp(NH2)-L-Ala-L-Phe-NHNH2 (XXIV), m. 190-200° (decomposition); [α]22D -60.5° ± 1° (c 1, 95% AcOH). Condensation of L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-NHNH2 (XXV) with XXII by the azide method gave 18% Me L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp(NH2)-L-Ala-L-Phe (XXVI), m. 180° (decomposition); [α]22D -62.5° ± 1° (c 1, 95% AcOH), -36° ± 1° (c 1, HCONMe2). The reaction of XXVI with N2H4.H2O gave 70% L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp(NH2)-L-Ala-L-Phe-NHNH2 (XXVII), m. 235° (decomposition); [α]22D -69.5° ± 1° (c 1, 95% AcOH). Condensation of N-benzyl-L-Pyr-L-Pro-L-Ser-L-Nor-NHNH2 (XXVIII) with XXII by the azide method gave 55% Me

N-benzyl-L-Pyr-L-Pro-L-Ser-L-Nor-L-Asp(NH2)-L-Ala-L-Phe (XXIX), m. 180°; [α]22D -64° ± 1° (c 2, 95% AcOH), -43° ± 1° (c 2, HCONMe2). The reaction of XXIX with N2H4.H2O gave 80% N-benzyl-L-Pyr-L-Pro-L-Ser-L-Nor-L-Asp(NH2)-L-Ala-L--Phe-NHNH2 (XXX), m. 230° (decomposition); [α]22D -72° ± 1° (c 2, 95° AcOH). Condensation of VII with Gly-L-Leu-L-Met-Gly-NH2 by the azide method gave 40% N-CTB-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-Gly-NH2 (XXXI), m. 250° (decomposition); [α]22D -39° ± 1° (c 1, 95% AcOH), -25.5° ± 1° (c 1, HCONMe2). The reaction of XXXI with CF3CO2H gave 95% L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-Gly-NH2.CF3CO2H, m. 250° (decomposition); [α]22D -27.5° ± 1° (c 1, 95% AcOH). Condensation of Nα, 1 Nε-(CTB)2-L-Lys-OC6H4NO2-p with XIV gave 59% Nα,1 Nε-(CTB)2-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (XXXII), m. 250° (decomposition); [α]22D -38.5° ± 1° (c 1, 95% AcOH). The reaction of XXXII with CF3CO2H gave 100% L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.2CF3CO2H, m. 220° (decomposition); [α]22D -26.5° ± 1° (c 1, 95% AcOH). Condensation of I with L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (XXXIII) by the azide method gave 43% N-CTB-L-Pro-L-Ser-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (XXXIV), m. 260° (decomposition); [α]22D -54.0° ± 1° (c 1, 95% AcOH). The reaction of XXXIV with CF3CO2H gave 90% L-Pro-L-Ser-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 240° (decomposition); [α]22D -49° ± 1° (c 1, 95% AcOH). Condensation of N-benzyl-L-Pyr-NHNH2 with XIV by the azide method gave 75% N-benzyl-L-Pyr-L-Asp- L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2, m. 260° (decomposition); [α]22D -36.5° ± 1° (c 1, 95% AcOH). Condensation of I with XIV by the azide method gave 74% N-CTB-L-Pro-L-Ser-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (XXXV), m. 200° (decomposition); [α]22D -36.6° ± 1° (c 1, 95% AcOH). The reaction of XXXV with CF3CO2H gave 90% L-Pro-L-Ser-L-Asp-L-Ala-L-Phe-L-Ilev-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 250° (decomposition); [α]22D -46° ± 1° (c 1, 95% AcOH). Condensation of XIX with XXXIII by the azide method gave 64% N-CTB-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (XXXVI), m. 260° (decomposition); [α]22D -49.5° ± 1° (c 1, 95% AcOH). The reaction of XXXVI with CF3CO2H gave 90% L-Pro-L-Ser-L-Lys-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.2C- F3CO2H, m. 215° (decomposition); [α]22D -48° ± 1° (c 1, 95% CF3CO2H), -41° ± 1° (c 1, 95% AcOH). Condensation of IV with XXXIII by the azide method gave 31.5% N-CTB-L-Pro-L-Ser-Nε-(N-CTB-L-Pro-L-Ser)-L-Lys-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (XXXVII), m. 200-10° (decomposition); [α]22D -66° ± 1° (c 1, 95% AcOH). The reaction of XXXVII with CF3CO2H gave 94% L-Pro-L-Ser-Nε-(L-Pro-L-Ser)-L-Lys-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met.2CF3CO2H, m. 250° (decomposition); [α]22D - 44° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Pro-L-Ser-L-Nor-NHNH2 (XXXVIII) with XXXIII by the azide method gave 71% N-CTB-L-Pro-L-Ser-L-Nor-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (XXXIX), m. 270° (decomposition); [α]22D -56° ± 1° (c 1, 95% AcOH). The reaction of XXXIX with CF3CO2H gave 94% L-Pro-L-Ser-L-Nor-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 220° (decomposition); [α]22D -46° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Pro-L-Ser-L-Nor-NHNH2 (XL) with XXXIII by the azide method gave 55% N-CTB-L-Pro-L-Ser-L-Nor-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (XLI), m. 265° (decomposition); [α]22D -39° ± 1° (c 1, 95% AcOH). The reaction of XLI with C3FCO2H gave 92% L-Pro-L-Ser-L-Nor-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 230° (decomposition); [α]22D -47° ± 1° (c 1, 95% AcOH). Condensation of N-benzyl-L-Pyr-Nε-CTB-L-Lys-NH-NH2 with XIV by the azide method gave 61% N-benzyl-L-Pyr-Nε-CTB-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met- NH2 (XLII), m. 250° (decomposition); [α]22D -28.5° ± 1° (c 1, 95% AcOH). The reaction of XLII with

CF_3CO_2H gave 92% N-benzyl-L-Pyr-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met- $NH_2.CF_3CO_2H$, m. 210° (decomposition); $[\alpha]_D^{22}$ -30° ± 1° (c 1,95% AcOH). Condensation of XXV with L-Asp-L-Ala-L-Phe-L-Ileu-L-Met-$NH_2.CF_3CO_2H$ by the azide method gave 42% L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-L-Met-NH_2 (XLIII), m. 240-50° (decomposition); $[\alpha]_D^{22}$ -69.5° ± 1° (c 1, 95% AcOH). The reaction of XLIII with CF_3CO_2H gave 73% L-Pyr-L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-L-Met-$NH_2.CF_3CO_2H$, m. 180° (decomposition); $[\alpha]_D^{22}$ -63.5° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Ser-Nε-CTB-L-Lys-$NHNH_2$ with XIV by the azide method gave 73% N-CTB-L-Ser-Nε-CTB-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH_2 (XLIV), m. 250° (decomposition); $[\alpha]_D^{22}$ -37.5° ± 1° (c 1, 95% AcOH). The reaction of XLIV with CF_3CO_2H gave 95% L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-$NH_2.2CF_3CO_2H$, m. 250° (decomposition); $[\alpha]_D^{22}$ -31.5° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Ala-L-Phe-L-Ala-$NHNH_2$ with XIV by the azide method gave 54% N-CTB-L-Ala-L-Phe-L-Ala-LAsp- L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH_2 (XLV), m. 250° (decomposition); $[\alpha]_D^{22}$ -39.5° ± 1° (c 1, 95% AcOH). The reaction of XLV with CF_3CO_2H gave 85% L-Ala-L-Phe-L-Ala-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met.CF_3CO_2H, m. 250° (decomposition); $[\alpha]_D^{22}$ -27° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Ala-L-Ser-Nε-CTB-L-Lys-L-Asp(NH2)-L-Ala-L-Phe-$NHNH_2$ with XI by the azide method gave 38% N-CTB-L-Ala-L-Ser-Nε-CTB-L-Lys-L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH_2 (XLVI), m. 260° (decomposition); $[\alpha]_D^{22}$ -35° ± 1° (c 1 95% AcOH). The reaction of XLVI with CF_3CO_2H gave 87% L-Ala-L-Ser-L-Lys-L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-$NH_2.2CF_3CO_2H$, m. 240° (decomposition); $[\alpha]_D^{22}$ -30° ± 1° (c 1, 95% AcOH). Condensation of N-CBO-L-Glu(NH2)-L-Pro-L-Ser-Nε-CBO-L-Lys-$NHNH_2$ (XLVII) with L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-NH_2 (XLVIII) by the azide method gave 89% N-CBO-L-Glu(NH2)-L-Pro-L-Ser-Nε-CBO-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-NH_2 (XLIX), m. 150° (decomposition); $[\alpha]_D^{22}$ -48.5° ± 1° (c 2, 95% AcOH). Hydrogenation of XLIX gave 92% L-Glu(NH2)-L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu, m. 200° (decomposition); $[\alpha]_D^{22}$ -50° ± 1° (c 1, 95% AcOH). Condensation of XLVII with β-O-benzyl-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-OBN (L) [obtained in 50% from N-CBO-(β-O-benzyl)-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-OBN with 2N HBr in AcOH] by the azide method gave 97% N-CBO-L-Glu(NH2)-L-Pro-L-Ser-Nε-CBO-L-Lys-(β-O-benzyl)-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-OBN (LI), m. 130° (decomposition); $[\alpha]_D^{22}$ -45.5° ± 1° (c 1, 95% AcOH). Hydrogenation of LI gave 94% L-Glu(NH2)-L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu, m. 190° (decomposition); $[\alpha]_D^{22}$ -54.5° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Pro-L-Ser-L-Asp(NH2)-Nε-CTB-L-Lys-$NHNH_2$ with XXXIII by the azide method gave 47% N-CTB-L-Pro-L-Ser-L-Asp(NH2)-Nε-CTB-L-Lys-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH_2 (LII), m. 250° (decomposition); $[\alpha]_D^{22}$ -51° ± 1° (c 1, 95% AcOH). The reaction of LII with CF_3CO_2H gave 90% L-Pro-L-Ser-L-Asp(NH2)-L-Lys-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-$NH_2.2CF_3CO_2H$, m. 200° (decomposition); $[\alpha]_D^{22}$ -39° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp(NH2)-L-Ala-L-Phe-$NHNH_2$ with XI by the azide method gave 18% N-CTB-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH_2 (LIII), m. 260° (decomposition); $[\alpha]_D^{22}$ -49.5° ± 1° (c 1, 95% AcOH). The reaction of LIII with CF_3CO_2H gave 89% L-Pro-L-Ser-L-Lys-L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met.$2CF_3CO_2H$, m. 220° (decomposition); $[\alpha]_D^{22}$ -37.5° ± 1° (c 1, 95% AcOH). Condensation of XIX with XIV by the azide method gave 69% N-CTB-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH_2 (LIV), m. 250° (decomposition); $[\alpha]_D^{22}$ -47.5° ± 1° (c 1, 95% AcOH). The reaction of LIV with

CF3CO2H gave 89% L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.2CF3CO2H, m. 250° (decomposition); [α]22D -42.5° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Pro-L-Ser-Nε-CTB-L-Lys-L-But-NHNH2 with XXXIII by the azide method gave 71% N-CTB-L-Pro-L-Ser-Nε-CTB-L-Lys-L-But-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LV), m. 270° (decomposition); [α]22D -49.5° ± 1° (c 1, 95% AcOH). The reaction of LV with CF3CO2H gave 90% L-Pro-L-Ser-L-Lys-L-But-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.2CF3CO2H, m. 200° (decomposition); [α]22D -45.5° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Pro-L-Ser-L-Nle-L-Asp(NH2)-L-Ala-L-Phe-NHNH2 with XI by the azide method gave 26% N-CTB-L-Pro-L-Ser-L-Nle-L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LVI), m. 265° (decomposition); [α]22D -52.5° ± 1° (c 1, 95% AcOH).
The reaction of LVI with CF3CO2H gave 84% L-Pro-L-Ser-L-Nle-L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 240° (decomposition); [α]22D -47° ± 1° (c 1, 95% AcOH). Condensation of XXXVIII with XIV by the azide method gave 53% N-CTB-L-Pro-L-Ser-L-Nle-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LVII), m. 270° (decomposition); [α]22D -55° ± 1° (c 1, 95% AcOH). The reaction of LVII with CF3CO2H gave 80% L-Pro-L-Ser-L-Nle-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 230° (decomposition); [α]22D -49° ± 1° (c 1, 95% AcOH). Condensation of XL with XIV by the azide method gave 73% N-CTB-L-Pro-L-Ser-L-Nor-L-Asp-L-Ala-L-Phe-L-IleuGly-L-Leu-L-Met-NH2 (LVIII), m. 260° (decomposition); [α]22D -60° ± 1° (c 1, 95% AcOH). The reaction of LVIII with CF3CO2H gave 85% L-Pro-L-Ser-L-Nor-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 180° (decomposition); [α]22D -49° ± 1° (c 1, 95% AcOH). Condensation of VI with XIV by the azide method gave 84% N-benzyl-L-Pyr-L-Pro-Nε-(N-benzyl-L-Pyr)-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2, m. 240° (decomposition); [α]22D -48° ± 1° (c 1, 95% AcOH).
Condensation of XXI with XXXIII by the azide method gave 28% N-benzyl-L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LIX), m. 250° (decomposition); [α]22D 53.5° ± 1° (c 1, 95% AcOH).
The reaction of LIX with F3CCO2H gave 88% N-benzyl-L-Pyr-L-Pro-L-Ser-L-Lys-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 220° (decomposition); [α]22D -52° ± 1° (c 1, 95% AcOH). Condensation of N-benzyl-L-Pyr-L-Pro-L-Ser-Nε-CBO-L-Lys-NHNH2 (LX) with XLVIII by the azide method gave 95% N-benzyl-L-Pyr-L-Pro-L-Ser-Nε-CBO-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-NH2 (LXI), m. 160° (decomposition); [α]22D -48.5° ± 1° (c 1, 95% AcOH). The hydrogenation of LXI gave 83% N-benzyl-L-Pyr L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-NH2 m. 185° (decomposition); [α]22D -49.5° ± 1° (c 1, 95% AcOH). Condensation of LX with L by the azide method gave 98% N-benzyl-L-Pyr-L-Pro-L-Ser-Nε-CBO-L-Lys-β-O-benzyl-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-OBN (LXII), m. 135° (decomposition); [α]22D -48.5° ± 1° (c 1, 95% AcOH). Hydrogenation of LXII gave 93% N-benzyl-L-Pyr-L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu, m. 240° (decomposition); [α]22D -57.5° ± 1° (c 1, 95% AcOH). Condensation of XXV with L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-NH2 by the azide method gave 80% L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-NH2 (LXIII), m. 260° (decomposition); [α]22D -63.5° ± 1° (c 1, 95% AcOH). The reaction of LXIII with CF3CO2H gave 89% L-Pyr-L-Pro-L-Ser-L-Lys-L-Ala-L-Phe-L-Ileu-Gly L-Leu-NH2.CF3CO2H, m. 210° (decomposition); [α]22D -59° ± 1° (c 1, 95% AcOH). Condensation of L-Pyr-L-Pro-L-Ser-Nε-CBO L-Lys-NHNH2 (LXIV) with L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly L-Leu-OBN by the azide method gave 93% L-Pyr-L-Pro-L-Ser Nε-CB O-L-Lys-L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-OBN (LXV), m. 225° (decomposition); [α]22D -59.5° ± 1° (c 1 95% AcOH).
Hydrogenation of LXV gave 90% L-Pyr-L-Pro-L- Ser-L-Lys-L-Asp(NH2)-L-Ala-L-

Phe-L-Ileu-Gly-L-Leu, m. 24° (decomposition); [α]22D -59° ± 1° (c 1, 95% AcOH). Condensation of LXIV with XLVIII by the azide method gave 87% L-Pyr L-Pro-L-Ser-Nε-CBO-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-NH2 (LXVI), m. 220° (decomposition); [α]22D -59.5° ± 1° (c 1, 95% AcOH). Hydrogenation of LXVI gave 57% L-Pyr-L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-NH2, m. 210° (decomposition); [α]22D -58.5° ± 1° (c 1, 95% AcOH). Condensation of LXIV with L by the azide method gave 97% L-Pyr-L-Pro-L-Ser-Nε-CBO-L-Lys-(β-O-benzyl)-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-OBN (LXVII), m. 175° (decomposition); [α]22D -56° ± 1° (c 1, 95% AcOH). Hydrogenation of LXVII gave 79% L-Pyr-L-Pro-L-Ser-L-Lys-L-Ala-L-Phe-L-Ileu-Gly-L-Leu, m. 250° (decomposition); [α]22D -65° ± 1° (c 1, 95% AcOH). Condensation of N-benzyl-L-Pyr-L-Ser-Nε-CTB-L-Lys-NHNH2 with XIV by the azide method gave 58% N-benzyl-L-Pyr-L-Ser-Nε-CTB-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LXVIII), m. 260° (decomposition); [α]22D -35.5° ± 1° (c 1, 95% AcOH). The reaction of LXVIII with CF3CO2H gave 89% N-benzyl-L-Pyr-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 200° (decomposition); [α]22D -35.5° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Glu(NH2)-L-Pro-L-Ser-Nε-CTB-L-Lys-NHNH2 with XIV by the azide method gave 66.5% N-CTB-L-Glu(NH2)-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LXIX), m. 220° (decomposition); [α]22D -51° ± 1° (c 1, 95% AcOH). The reaction of LXIX with CF3CO2H gave 90% L-Glu(NH2)-L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.2CF3CO2H, m. 200° (decomposition); [α]22D -53° ± 1° (c 1, 95% AcOH). Condensation of N-CTB-L-Glu-L-Pro-L-Ser-Nε-CTB-L-Lys-NHNH2 with XIV by the azide method gave 72% N-CTB-L-Glu-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LXX), m. 220-50° (decomposition); [α]22D -56° ± 1° (c 1, 95% AcOH). The reaction of LXX with CF3CO2H gave 88% L-Glu-L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-L-Leu-Gly-L-Leu-L-Met-NH2.2CF3CO2H, m. 200° (decomposition); [α]22D -43.5° ± 1° (c 1, 95% AcOH). Condensation of N-benzyl-L-Pyr-L-Pro-L-Ser-L-Asp(NH2)-Nε-CTB-L-Lys-NHNH2 with XXXIII by the azide method gave 51% N-benzyl-L-Pyr-L-Pro-L-Ser-L-Asp(NH2)-Nε-CTB-L-Lys-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LXXI), m. 250° (decomposition); [α]22D -51° ± 1° (c 1, 95% AcOH). The reaction of LXXI with CF3CO2H gave 91% N-benzyl-L-Pyr-L-Pro-L-Ser-L-Asp(NH2)-L-Lys- L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 200° (decomposition); [α]22D -52.5° ± 1° (c 1, 95% AcOH). Condensation of XXIV with XI by the azide method gave 46% N-benzyl-L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LXXII), m. 265° (decomposition); [α]22D -57° ± 1° (c 1, 95% AcOH). The reaction of LXXII with CF3CO2H gave 91% N-benzyl-L-Pyr-L-Pro-L-Ser-L-Lys-L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 220° (decomposition); [α]22D -53.5° ± 1° (c 1, 95% AcOH). Condensation of XXI with XIV by the azide method gave 96% N-benzyl-L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LXXIII), m. 250°(decomposition); [α]22D -53.5° ± 1° (c 1, 95% AcOH). The reaction of LXXIII with CF3CO2H gave 45% N-benzyl-L-Pyr-L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H (N-benzyleledoisin-CF3CO2H), m. 220° (decomposition); [α]22D -48° ± 1° (c 1, 95% AcOH). Condensation of XXVII with XI by the azide method gave 56% L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp(NH2)- L- Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LXXIV), m. 265° (decomposition); [α]22D -66° ± 1° (c 0.5, 95% AcOH). The reaction of LXXIV with CF3CO2H gave 84% L-Pyr-L-Pro-L-Ser-L-Lys-L-Asp(NH2)L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 195° (decomposition) Condensation of XXV with XIV by the azide method gave 81% L-Pyr-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-

L-Met-NH2 (LXXV), m. 230° (decomposition); [α]22D -61° ± 1° (c 2, 95% AcOH). The reaction of LXXV with CF3CO2H gave 93% L-Pyr-L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H (eledoisin trifluoro- acetate) (LXXVI), m. 200-10° (decomposition); [α]22D -59° ± 1° (c 1, 95% AcOH). Countercurrent extraction of LXXVI with secBuOH-0.1N NH4OH gave L-Pyr-L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met (eledoisin), m. 230°; [α]22D -44° ± 1° (c 1, 95% AcOH). Condensation of XXX with XI by the azide method gave 37% N-benzyl-L-Pyr-L-Pro-L-Ser-L-Nle- L-Asp(NH2)-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2, m. 270°; [α]22D -62° ± 1° (c 1, 95% AcOH). Condensation of XXVIII with XIV by the azide method gave 69% N-benzyl-L-Pyr-L-ProL-Ser-L-Nle-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2, m. 250° (decomposition); [α]22D -41° ± 1° (c 1, 95% AcOH), -34° ± 1° (c 1, HCONMe2). Condensation of N-benzyl-L-Pyr-L-Pro-L-Ser-L-Nor-NHNH2 with XIV by the azide method gave 62.5% N-benzyl-L-Pyr-L-Pro-L-Ser-L-Nor-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2, m. 220-40° (decomposition); [α]22D = -60° ± 1° (c 1, 95% AcOH). Condensation of N-benzyl-L-Pyr-L-Glu(NH2)-L-Pro-L-Ser-Nε-CTB-L-Lys-NHNH2 with XIV by the azide method gave 79% N-benzyI-L-Pyr-L-Glu(NH2)-L-Pro-L-Ser-Nε-CTB-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2 (LXXVII), m. 220-30° (decomposition); [α]22D -52.5° ± 1° (c 1, 95% AcOH). The reaction of LXXVII with CF3CO2H gave 89% N-benzyl-L-Pyr-L-Glu(NH2)-L-Pro-L-Ser-L-Lys-L-Asp-L-Ala-L-Phe-L-Ileu-Gly-L-Leu-L-Met-NH2.CF3CO2H, m. 200° (decomposition); [α]22D -52° ± 1° (c 1, 95% AcOH).

IT Acetic acid, trifluoro-, compound with eledoisin (1:1)
Acetic acid, trifluoro-, compound with N-benzy-L-5-oxoprolyl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-L-methioninamide (1:1)
Acetic acid, trifluoro-, compound with L-alanyl-L-seryl-L-lysyl-L-asparaginyl-L-alany-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-L-methioninamide (2:1)
Acetic acid, trifluoro-, compound with L-asparaginyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-L-methioninamide
Acetic acid, trifluoro-, compound with L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-L-α -**aminobutyramide** (1:1)
Acetic acid, trifluoro-, compound with L-lysyl-L-aspartyl-L-alanyl-L-phenyl-alanyl-L-isoleucylglycyl-L-leucyl-L-methioninamide (2:1)
Acetic acid, trifluoro-, compound with L-prolyl-L-seryl-N-(L-prolyl-L-Seryl)-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-L-methioninamide (2:1)
Acetic acid, trifluoro-, compound with L-prolyl-L-seryl-L-alanyl-L-phenyl-alanyl-L-isoleucyglycyl-L-leucyl-L-methioninamide (1:1)
Acetic acid, trifluoro-, compound with L-prolyl-L-seryl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-L-methioninamide (2:1)
Acetic acid, trifluoro-, compound with L-prolyl-L-seryl-L-lysyl-L-α-aminobutyryl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-L-methioninamide (2:1)
Alanine, N-[N-[N2-[N-[N-[1-(1-benzyl-5-oxo-L-prolyl)-L-prolyl]-L-seryl]-L-norleucyl]-L-asparaginyl]-L-alanyl]-3-phenyl-, hydrazide, L-
Alanine, N-[N-[N2-[N-[N-[1-(1-benzyl-5-oxo-L-prolyl)-L-prolyl]-L-seryl]-L-norleucyl]-L-asparaginyl]-L-alanyl]-3-phenyl-, methyl ester L-
Alanine, N-[N-[N2-[N6-carboxy-N2-[N-[1-(5-oxo-L-prolyl)-L-prolyl]-L-seryl]-L-lysyl]-L-asparaginyl]-L-alanyl]-3-phenyl-, N-tert-butyl Me ester, L-
Butyramide, L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-α-amino-, trifluoroacetate (1:1), L-
Glycinamide, N-carboxy-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-L-methionyl-, tert-butyl ester
Leucinamide, N-benzyl-L-5-oxoprolyl-L-prolyl-L-seryl-Nε-carboxy-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-, tert-butyl ester, L-

Leucinamide, L-5-oxoprolyl-L-prolyl-L-seryl-L-lysyl-L-asparaginyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-, trifluoroacetate (salt), L-

Leucine, N-[N-[N-[N-[N-[N-[N6-carboxy-N2-[N-[1-(5-oxo-L-prolyl)-L-prolyl]-L-seryl]-L-lysyl]-L-α-aspartyl]-L-alanyl]-3-phenyl-L-alanyl]-L-isoleucyl]glycyl]-, dibenzyl p-nitrobenzyl ester, L-

Lysine, N6-(1-benzyl-5-oxo-L-prolyl)-N2-[1-(1-benzyl-5-oxo-L-prolyl)-L-prolyl]-, hydrazide, L-

Lysine, N6-(1-benzyl-5-oxo-L-prolyl)-N2-[1-(1-benzyl-5-oxo-L-prolyl)-L-prolyl]-, methyl ester, L-

Lysine, N6-carboxy-N2-[N-(1-carboxy-L-prolyl)-L-seryl]-, benzyl tert-Bu Me ester, L-

Methioninamide, 1-benzyl-5-oxo-L-prolyl-L-prolyl-L-seryl-L-norvalyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, L-

Methioninamide, carboxy-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, tert-butyl ester, S-oxide, L-

Methioninamide, prolylseryllysylisoleucylglycylleucyl-, bis(trifluoroacetate) (salt), L-

Methioninamide, N-benzyl-L-5-oxoprolyl-Nε-carboxy-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, tert-butyl ester, L-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, L-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-glutaminyl-L-prolyl-L-seryl-Nε-carboxy-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-glutaminyl-L-prolyl-L-seryl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalalnyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate, L-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate, L-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-prolyl-L-seryl-Nε-carboxy-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, L-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-prolyl-L-seryl-Nε-carboxy-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, tert-butyl ester, L-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-prolyl-L-seryl-L-asparaginyl-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate, L-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-prolyl-L-seryl-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate, L-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-prolyl-L-seryl-L-lysyl-L-asparaginyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate, L-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-prolyl-L-seryl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate, L-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-prolyl-L-seryl-L-norleucyl-L-aspartyl-L-alanyl-L-phenyl-alanyl-L-isoleucylglycyl-L-leucyl-, L-

Methioninamide, N-benzyl-L-5-oxoprolyl-L-seryl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate (salt), L-

Methioninamide, N-carboxy-L-prolyl-L-seryl-Nε-(N-carboxy-L-prolyl-L-seryl)-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, di-tert-butyl ester, L-

Methioninamide, N-carboxy-L-prolyl-L-seryl-Nε-carboxy-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, tert-butyl ester, L-

Methioninamide, N-carboxy-L-prolyl-L-seryl-Nε-carboxy-L-lysyl-L-isoleucylglycyl-L-leucyl-, di-tert-butyl ester, L-

Methioninamide, N-carboxy-L-prolyl-L-seryl-Nε-carboxy-L-lysyl-L-isoleucylglycyl-L-leucyl-, di-tert-butyl ester, L-

Methioninamide, N-carboxy-L-prolyl-L-seryl-L-asparaginyl-Nε-carboxy-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, di-tert-butyl ester, L-

Methioninamide, N-carboxy-L-prolyl-L-seryl-L-aspartyl-L-alanyl-L-

phenylalanyl-L-isoleucylglycyl-L-leucyl-, tert-butyl ester, L-
Methioninamide, N-carboxy-L-prolyl-L-seryl-L-norvalyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, tert-butyl ester, L-
Methioninamide, N-carboxy-L-prolyl-L-seryl-L-norvalyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, tert-butyl ester, L-
Methioninamide, Nα,Nε-dicarboxy-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, di-tert-butyl ester, L-
Methioninamide, N2-carboxy-L-asparaginyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, tert-butyl ester, L-
Methioninamide, L-5-oxoprolyl-L-prolyl-L-seryl-Nε-carboxy-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucyl-, tert-butyl ester, L-
Methioninamide, L-5-oxoprolyl-L-prolyl-L-seryl-Nε-carboxy-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, tert-butyl ester, L-
Methioninamide, L-5-oxoprolyl-L-prolyl-L-seryl-L-lysyl-L-asparaginyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate (salt), L-
Methioninamide, L-5-oxoprolyl-L-prolyl-L-seryl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucyl-, trifluoroacetate (salt), L-
Methioninamide, L-alanyl-L-phenylalanyl-L-alanyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate, L-
Methioninamide, L-alanyl-L-seryl-L-lysyl-L-asparaginyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, bis(trifluoroacetate), L-
Methioninamide, L-asparaginyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate, L-
Methioninamide, L-aspartyl-L-alanyl-L-phenylalanyl-L-leucylglycyl-L-leucyl-, trifluoroacetate, L-
Methioninamide, L-aspartyl-L-alanyl-L-phenylalanyl-L-leucylglycyl-L-leucyl-, S-oxide, trifluoroacetate, L-
Methioninamide, L-aspartyl-L-alanyl-L-phenylalanyl-L-leucylglycyl-L-leucyl-, S-oxide, L-
Methioninamide, L-glutaminyl-L-prolyl-L-seryl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, L-
Methioninamide, L-glutamyl-L-prolyl-L-seryl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, bis(trifluoroacetate) (salt), L-
Methioninamide, L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, bis(trifluoroacetate), L-
Methioninamide, L-prolyl-L-seryl-Nε-(L-prolyl-L-seryl)-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, bis(trifluoroacetate) (salt), L-
Methioninamide, L-prolyl-L-seryl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate (salt), L-
Methioninamide, L-prolyl-L-seryl-L-asparaginyl-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, bis(trifluoroacetate) (salt), L-
Methioninamide, L-prolyl-L-seryl-L-asparaginyl-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, L-
Methioninamide, L-prolyl-L-seryl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate (salt), L-
Methioninamide, L-prolyl-L-seryl-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, bis(trifluoroacetate) (salt), L-
Methioninamide, L-prolyl-L-seryl-L-lysyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, L-
Methioninamide, L-prolyl-L-seryl-L-lysyl-L-asparaginyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, bis(trifluoroacetate) (salt), L-
Methioninamide, L-prolyl-L-seryl-L-lysyl-L-asparaginyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, L-
Methioninamide, L-prolyl-L-seryl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, bis(trifluoroacetate) (salt), L-
Methioninamide, L-prolyl-L-seryl-L-lysyl-L-aspartyl-L-alanyl-L-

phenylalanyl-L-isoleucylglycyl-L-leucyl-, L-
Methioninamide, L-prolyl-L-seryl-L-lysyl-L-α-aminobutyryl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, bis(trifluoroacetate) (salt), L-
Methioninamide, L-prolyl-L-seryl-L-lysyl-L-α-aminobutyryl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, L-
Methioninamide, L-prolyl-L-seryl-L-norleucyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate (salt), L-
Methioninamide, L-prolyl-L-seryl-L-norleucyl-L-asparaginyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate (salt), L-
Methioninamide, L-prolyl-L-seryl-L-norleucyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate (salt), L-
Methioninamide, L-prolyl-L-seryl-L-norvalyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate (salt), L-
Methioninamide, L-prolyl-L-seryl-L-norvalyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate (salt), L-
Methioninamide, L-prolyl-L-seryl-L-norvalyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, L-
Methioninamide, L-seryl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, bis(trifluoroacetate) (salt), L-
Methioninamide, L-seryl-L-lysyl-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, L-
Methionine, N-[N-[N-[N-[N-(N-L-α-aspartyl-L-alanyl)-3-phenyl-L-alanyl]-L-isoleucyl]glycyl]-L-leucyl]-, trifluoroacetate, L-
Norvalinamide, N-carboxy-L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, tert-butyl ester, L-
Norvalinamide, L-aspartyl-L-alanyl-L-phenylalanyl-L-isoleucylglycyl-L-leucyl-, trifluoroacetate, L-

L28 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1963:469438 CAPLUS
DOCUMENT NUMBER: 59:69438
ORIGINAL REFERENCE NO.: 59:12921b-e
TITLE: α-Amino acid amide hydrohalides
INVENTOR(S): Johnson, Hubert E.; Crosby, Donald G.
PATENT ASSIGNEE(S): Union Carbide Corp.
SOURCE: 35 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1325982		19630503	FR	
GB 990392			GB	
GB 990393			GB	
US 3190917		1965	US	
PRIORITY APPLN. INFO.:			US	19610608

AB Alc. solns. of C3-22 aliphatic α-aminonitriles are treated with HCl, HBr, or HI to give the title compds. Thus, a solution of 50 g. Me2CH(NH2)CN in 500 ml. absolute EtOH is saturated with dry HCl at 20-5°, and the mixture stirred for 16 hrs. at 20-5°, refluxed for 1 hr., and cooled to give 58 g. valinamide-HCl, m. 246-9° (decomposition) (EtOH), 76% yield. Similarly prepared are (m.p. given): glycinamide-HCl, 180-7° (decomposition); alaninamide-HCl, 159-66° (decomposition); leucinamide-HCl, 224-9° (decomposition) (EtOH); phenylalaninamide-HCl, 238-41° (decomposition) (EtOH); valinamide-HBr, 235-8° (decomposition) (EtOH); α-methylalaninamide- HCl, 268° (decomposition) (EtOH); . **alpha.-aminobutyramide**-HCl, 218-22° (decomposition) (HOAc); norvalinamide-HCl, 250° (decomposition) (EtOH); isoleucinamide-HCl, 232-4° (decomposition) (HOAc); phenylglycinamide-HCl, 270-3° (decomposition) (EtOH); p-chlorophenylglycinamide-HCl,

250-67° (EtOH); serinamide-HCl, 196-9° (decomposition) (EtOH); o-ethylserinamide-HCl, 165-6° (decomposition) (iso-PrOH); methioninamide-HCl, 160-2° (decomposition) (EtOH); N-(carboxamidomethyl)morpholine - HCl, 192-5° (EtOH); 1-methyl-2,6-dicarboxamidopiperidine-HCl, 281-2° (decomposition); α-methyl-α-phenylglycinamide-HCl, 266-7° (HOAc); sarcosinamide-HCl,160-2° (decomposition) (EtOH).

AB Alc. solns. of C3-22 aliphatic α-aminonitriles are treated with HCl, HBr, or HI to give the title compds. Thus, a solution of 50 g. Me2CH(NH2)CN in 500 ml. absolute EtOH is saturated with dry HCl at 20-5°, and the mixture stirred for 16 hrs. at 20-5°, refluxed for 1 hr., and cooled to give 58 g. valinamide-HCl, m. 246-9° (decomposition) (EtOH), 76% yield. Similarly prepared are (m.p. given): glycinamide-HCl, 180-7° (decomposition); alaninamide-HCl, 159-66° (decomposition); leucinamide-HCl, 224-9° (decomposition) (EtOH); phenylalaninamide-HCl, 238-41° (decomposition) (EtOH); valinamide-HBr, 235-8° (decomposition) (EtOH); α-methylalaninamide- HCl, 268° (decomposition) (EtOH); . **alpha.-aminobutyramide**-HCl, 218-22° (decomposition) (HOAc); norvalinamide-HCl, 250° (decomposition) (EtOH); isoleucinamide-HCl, 232-4° (decomposition) (HOAc); phenylglycinamide-HCl, 270-3° (decomposition) (EtOH); p-chlorophenylglycinamide-HCl, 250-67° (EtOH); serinamide-HCl, 196-9° (decomposition) (EtOH); o-ethylserinamide-HCl, 165-6° (decomposition) (iso-PrOH); methioninamide-HCl, 160-2° (decomposition) (EtOH); N-(carboxamidomethyl)morpholine - HCl, 192-5° (EtOH); 1-methyl-2,6-dicarboxamidopiperidine-HCl, 281-2° (decomposition); α-methyl-α-phenylglycinamide-HCl, 266-7° (HOAc); sarcosinamide-HCl,160-2° (decomposition) (EtOH).

L28 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1963:448691 CAPLUS
DOCUMENT NUMBER: 59:48691
ORIGINAL REFERENCE NO.: 59:8871b-e
TITLE: Synthetic peptides related to eledoisin
AUTHOR(S): Camerino, B.; De Caro, G.; Boissonnas, R. A.; Sandrin, Ed.; Sturmer, E.
CORPORATE SOURCE: Farmitalia, Milan
SOURCE: Experientia (1963), 19, 339-42
CODEN: EXPEAM; ISSN: 0014-4754
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The following list of analogs and partial sequences related to eledoisin were reported [compound, m.p. (decomposition), [α]22D (1 g. 95% AcOH), and electrophoretic mobility vs. Try in 80% HCO2H given]: R-Pyroglu-Pro-Ser-Lys-Asp(R')-Ala-Phe-Ileu-Gly-Leu (I) [R =H, R' = OH(II)], 250°, -65°, 0.60; II amide, 210°, -59°, 0.53; I [R = Bz, R' = OH (III)], 240°, -58°, 0.55; III amide, 185°, -50°, 0.55; I [R = H, R' = NH2 (IV)], 240°, -59°, 0.48; IV amide, 210°, -59°, 0.54; H-Glu(NH2)-Pro-Ser-Lys-Asp(OH)-Ala-Phe-Ileu-Gly-Leu (V), 190°, -55°, 0.85; V amide, 200°, -50°, 0.86; H-Asp(R)-Ala-Phe-Ileu-Gly-Leu (VI) [R = OH (VIII)], 250°, -29°, 0.65; VII amide, 250°, -30°, 0.65; VI [R = H, R = NH2 (VIII)], 240°, -28°, 0.68; VIII amide, 260°, -30°, 0.68; H-Asp(OH)-Ala-Phe-Ileu-Gly-Leu-Met-Gly-NH2, 250°, -27°, 0.63; H-Asp(OH)-Ala-Phe-Ileu-Gly-Leu-Met, 250, -30, 0.61; H-Asp(OH)-Ala-Phe-Ileu-Gly-Leu-Met(:O)-NH2, 240°, -22°, 0.62; H-Asp(OH)-Ala-Phe-Ileu-Gly-Leu-α - **aminobutyramide**, 260°, -33°, 0.61; H-Asp-(OH)-Ala-Phe-Ileu-Gly-Leu-Norval-NH2, 260°, -32°, 0.60; H-Asp(OH)-Ala-Phe-Ileu-Gly-Leu-Norleu-NH2, 260°, -34°, 0.57; H-Ala-Phe-Ileu-Gly-Leu-Met-NH2, 225°, -25°, 0.58; H-Ala-Phe-Ileu-Gly-Leu-Met-Met-NH2, 300°, -39°, 0.58;

H-Ala-Phe-Ileu-Gly-Leu-Leu-NH2, 230°, -37°, 0.54; H-Ala-Phe-Ileu-Gly-Leu-Val-NH2, 310°, -25°, 0.62; H-Ala-Phe-Ileu-Gly-Leu-D-Val-NH2, 290°, -18°, 0.63; H-Ala-Phe-Ileu-Gly-Met-Met-NH2, 300°, -20°, 0.61; H-Ala-Phe-Pro-Gly-Ileu-Met-NH2, 166°, -45°, 0.58; H-Ala-Phe-Pro-Gly-Leu-Met-NH2, 158°, -44°, 0.58; H-Ala-Gly-Ileu-Gly-Leu-Met-NH2, 199°, -14°, 0.63; H-Phe-Ileu-Gly-Leu-Met-NH2, 170°, -14°, 0.64; H-Pro-Ser-Lys-Ileu-Gly-Leu-Met-NH2, 150°, -44°, 1.00; H-Ser-Lys-Ileu-Gly-Leu-Met-NH2, 160°, - 35°, 1.03; H-Pyroglu-Pro-Ser-Lys-Asp(OH)-Ala-Phe-Ileu-Gly, 190°, -66°, 0.45; H-Pyroglu-Pro-Ser-Lys-Asp(OH)-Ala-Phe-Ileu, 140°, -61°, 0.47. All these derivs. were found to be devoid or almost devoid of biol. activity.

AB The following list of analogs and partial sequences related to eledoisin were reported [compound, m.p. (decomposition), [α]22D (1 g. 95% AcOH), and electrophoretic mobility vs. Try in 80% HCO2H given]: R-Pyroglu-Pro-Ser-Lys-Asp(R')-Ala-Phe-Ileu-Gly-Leu (I) [R =H, R' = OH(II)], 250°, -65°, 0.60; II amide, 210°, -59°, 0.53; I [R = Bz, R' = OH (III)], 240°, -58°, 0.55; III amide, 185°, -50°, 0.55; I [R = H, R' = NH2 (IV)], 240°, -59°, 0.48; IV amide, 210°, -59°, 0.54; H-Glu(NH2)-Pro-Ser-Lys-Asp(OH)-Ala-Phe-Ileu-Gly-Leu (V), 190°, -55°, 0.85; V amide, 200°, -50°, 0.86; H-Asp(R)-Ala-Phe-Ileu-Gly-Leu (VI) [R = OH (VIII)], 250°, -29°, 0.65; VII amide, 250°, -30°, 0.65; VI [R = H, R = NH2 (VIII)], 240°, -28°, 0.68; VIII amide, 260°, -30°, 0.68; H-Asp(OH)-Ala-Phe-Ileu-Gly-Leu-Met-Gly-NH2, 250°, -27°, 0.63; H-Asp(OH)-Ala-Phe-Ileu-Gly-Leu-Met, 250, -30, 0.61; H-Asp(OH)-Ala-Phe-Ileu-Gly-Leu-Met(:O)-NH2, 240°, -22°, 0.62; H-Asp(OH)-Ala-Phe-Ileu-Gly-Leu-α - **aminobutyramide**, 260°, -33°, 0.61; H-Asp-(OH)-Ala-Phe-Ileu-Gly-Leu-Norval-NH2, 260°, -32°, 0.60; H-Asp(OH)-Ala-Phe-Ileu-Gly-Leu-Norleu-NH2, 260°, -34°, 0.57; H-Ala-Phe-Ileu-Gly-Leu-Met-NH2, 225°, -25°, 0.58; H-Ala-Phe-Ileu-Gly-Leu-Met-Met-NH2, 300°, -39°, 0.58; H-Ala-Phe-Ileu-Gly-Leu-Leu-NH2, 230°, -37°, 0.54; H-Ala-Phe-Ileu-Gly-Leu-Val-NH2, 310°, -25°, 0.62; H-Ala-Phe-Ileu-Gly-Leu-D-Val-NH2, 290°, -18°, 0.63; H-Ala-Phe-Ileu-Gly-Met-Met-NH2, 300°, -20°, 0.61; H-Ala-Phe-Pro-Gly-Ileu-Met-NH2, 166°, -45°, 0.58; H-Ala-Phe-Pro-Gly-Leu-Met-NH2, 158°, -44°, 0.58; H-Ala-Gly-Ileu-Gly-Leu-Met-NH2, 199°, -14°, 0.63; H-Phe-Ileu-Gly-Leu-Met-NH2, 170°, -14°, 0.64; H-Pro-Ser-Lys-Ileu-Gly-Leu-Met-NH2, 150°, -44°, 1.00; H-Ser-Lys-Ileu-Gly-Leu-Met-NH2, 160°, - 35°, 1.03; H-Pyroglu-Pro-Ser-Lys-Asp(OH)-Ala-Phe-Ileu-Gly, 190°, -66°, 0.45; H-Pyroglu-Pro-Ser-Lys-Asp(OH)-Ala-Phe-Ileu, 140°, -61°, 0.47. All these derivs. were found to be devoid or almost devoid of biol. activity.

L28 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1960:118220 CAPLUS
DOCUMENT NUMBER: 54:118220
ORIGINAL REFERENCE NO.: 54:22601d-h

TITLE: A novel reaction involving formamide

AUTHOR(S): Schipper, E.
CORPORATE SOURCE: Ethicon Inc., Somerville, NJ

SOURCE: Chemistry & Industry (London, United Kingdom) (1960) 464-5
CODEN: CHINAG; ISSN: 0009-3068
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 54:118220
GI For diagram(s), see printed CA Issue.
AB Heating 1-anilinocyclohexanecarboxamide (I) with HCONH2 (II) at 180-200° gave RN.CH2.NH.CO.CR'R'' (III) (R = Ph, R'R'' = C5H10) (IV), m. 199-200°, also obtained by catalytic reduction of 1-phenyl-1,3-diazaspiro[4.5]dec-2-en-4-one, m. 172-3°, prepared from I and Et orthoformate. Similarly prepared were the following III: R = p-MeC6H4, R'R'' = (CH2)5, m. 203-4°; R = p-ClC6H4, R'R'' = (CH2)5, m. 214-15°; and R = Me, R' = Et, R'' = Ph, m. 154-5°. 1-Aminocyclohexanecarboxamide and 2-phenyl-**2-aminobutyramide** with II gave the following III: R = CHO, R'R'' = (CH2)5 (V), m. 194-5°; and R = CHO, R' = Et, R'' = Ph, m. 166-7°. Mild hydrolysis of the last 2 III gave III [R = H, R'R'' = (CH2)5] and III (R = H, R' = Et, R'' = Ph), resp., which heated with II were reconverted to their 1-formyl derivs. II with H2NCH2CONPh2 gave III (R = CH: NH, R' = R'' = Ph), m. 264-5°, which was hydrolyzed to III (R = H, R' = R'' = Ph). Preliminary expts. indicated that simple α-amino acids and II did not give III, however 1-anilinocyclohexanecarboxylic acid gave IV. Et 1-methylaminocyclohexanecarboxylate and II gave VI (R = Me). The formation of III probably proceeded via a modified Leuckart mechanism, a concept which derived some support from the fact that heating VI (R = H) with II gave an excellent yield of V.
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L28 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1959:62340 CAPLUS
DOCUMENT NUMBER: 53:62340
ORIGINAL REFERENCE NO.: 53:11263d-i
TITLE: N,N-Dibenzylamino acids
INVENTOR(S): Anatol, J.; Torelli, V.
PATENT ASSIGNEE(S): U.C.L.A.F.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1109586		19560131	FR	

AB N,N-Dibenzyl-α-amino acids are prepared by treating an α-hydroxy nitrile with dibenzylamine to give the acid nitrile which is hydrolyzed in 2 steps to the acid. Thus, 53.25 g. lactonitrile refluxed 4 hrs. with

147.75 g. dibenzylamine (I) and 100 cc. EtOH gives 184.5 g. N,N-dibenzyl-α-propionitrile, m. 87° (EtOH); 720 cc. H2SO4 (66° B.acte.e.) added to the nitrile at 0° followed by heating 1 hr. at 100° gives, on basifying, 187.5 g. of the amide, m. 141-2° (1:1 aqueous EtOH). Refluxing the amide 72 hrs. with 1000 cc. HCl (d. 1.19) and 1 l. H2O gives 214 g. (PhCH2)2NCHMeCO2H.HCl[(PhCH2)2 NCHMeCO2H.2.5H2O, m. 115-20° (from 2 vols. hot H2O)]; 50 g. complex dissolved in 25 cc. H2O and 50 cc. 5N NaOH gives on acidifying with HOAc a solvated product dehydrated azeotropically with benzene or cyclohexane to N,N-dibenzyl-DL-alanine, m. 97-8° (cyclohexane), m. 80° (petr. ether); the forms are interchanged by dissolving in cyclohexane and seeding with the desired polymorph. α-Hydroxybutyronitrile (65 g.) with 150 g. I gives 202 g. dibenzylaminonitrile as an oil, hydrolyzed with H2SO4 to 201 g. N,N-dibenzyl-α -**aminobutyramide**, m. 123° (70% EtOH), which (110 g.) refluxed 72 hrs. with 1100 cc. 5N HCl, evaporated to dryness, taken up in EtOH, and neutralized to Congo red with pyridine gives, on adding a further 37 cc. to liberate the base, 81 g. N,N-dibenzyl-DL-α-aminobutyric acid (solvated form), m. 120-5°, m. 98° (nonsolvated) (isopropyl ether). Similarly 76 g. α-hydroxyvaleronitrile with 150 g. I gives 213 g. oil, hydrolyzed to 205 g. N,N-dibenzyl-α-aminovaleramide, m. 89° (petr. ether); 145 g. amide hydrolyzed with 1450 cc. 5N HCl and 200 cc. HOAc gives 116 g. N,N-dibenzyl-DL-norvaline, m. 125° (solvated), m. 83-5° (nonsolvated). The nonsolvated compound dissolved in Na2CO3 and precipitated with HOAc gives a product, m. 115-20°. α-Hydroxyisovaleronitrile gives successively N,N-dibenzyl-α-aminoisovaleronitrile, m. 113°, the corresponding amide, m. 144° (boiling EtOH) (hydrochloride m. 185-90°), and N,N-dibenzyl-DL-valine, m. 114-15° (petr. ether). α-Hydroxyisocapronitrile gives N,N-dibenzyl-α-aminoisocapronitrile, m. 60° (EtOH), the amide, m. 119-20° (cyclohexane), and N,N-dibenzylleucine, m. 99° (petr. ether). Cf. following abstract

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L28 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1959:56103 CAPLUS
DOCUMENT NUMBER: 53:56103
ORIGINAL REFERENCE NO.: 53:10055f-i,10056a-h
TITLE: Resolution of amino acids. I. Resolution of racemic phenylalanine and γ-phenyl-α-aminobutyric acid by leucine aminopeptidase
AUTHOR(S): Tanaka, Atsushi; Izumiya, Nobuo
CORPORATE SOURCE: Kyushu Univ., Fukuoka
SOURCE: Bulletin of the Chemical Society of Japan (1958), 31, 529-32
CODEN: BCSJA8; ISSN: 0009-2673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB cf. du Vigneaud and Irish, C.A. 32, 17641. DL-Phenylalaninamide (I) and DL-phenylamino-butyramide (II) were resolved to L-amino acids and D-amino acid amides by partially purified leucine aminopeptidase (III). A partially purified enzyme solution of III was prepared as described by Smith (cf. Spackman, et al., C.A. 49, 4754g). The rate of enzyme action on the amides was followed by measurement of the extent of NH3 liberated in Conway microdiffusion vessels (cf. Johnson, et al., C.A. 45, 3880c). The rate of hydrolysis (Cl + substrate concentration) of I and II with the enzyme preparation slightly increased with increase in concentration of the substrates. In the presence of Mn++) (0.0005 .apprx. 0.008M), an apparent increase of hydrolysis was observed in the case of I, with little corresponding effect with II. I.HCl, m. 234-6°, was synthesized from DL-phenylalanine Et ester-HCl in 95% yield by the method of Smith and Spackman (cf. C.A. 49, 4754h). DL-γ-Phenyl-α-aminobutyric acid (IV) was prepared by refluxing Et acetamidocyanoacetate, Na, and PhCH2CH2Br in EtOH, the precipitated salt filtered off, a small amount of AcOH added, the filtrate evaporated in vacuo to an oil which later crystallized on addition of H2O, the crystals collected, and washed with H2O to yield the Et ester, m. 116° (EtOH-H2O). This ester was refluxed with concentrated HCl to yield IV, m. 300-302° (decomposition), in 66% yield. IV (81 g.) in 1.5 l. EtOH was saturated at room temperature with dry HCl, the solution refluxed 1 hr., the solvent removed in vacuo, and the residue treated with dry Et2O to yield 98 g. DL-γ-phenyl-α-aminobutyric acid Et ester hydrochloride (V), m. 135-6° (EtOH-Et2O). II.HCl, m. 214-17° (decomposition) (MeOH-Et2O), was prepared from Vin 91% yield in the same way as L-phenylalaninamide hydrochloride. The resolution of I was achieved by dissolving 45.2 g. of its hydrochloride in 1.5 l. H2O containing 0.224 g. MnCl2.6H2O, adjusting the pH to 7.5 with N aqueous NH4OH, adding the enzyme solution containing the equivalent of 2.25 mg. protein N, making up the volume to 2.25 l., and incubating the solution 40 hrs. at 38°; NH3 determination indicated complete hydrolysis of the L-isomer, and the pH of the solution was 6.5. The remaining clear solution was passed through a column of Amberlite IRA-400 in the alkaline phase and 8 l. H2O added to the top of the column. Detection of the amide and NH3 in the fractions was made with Nessler reagent or the ninhydrin spot test on paper. The fractions were combined and evaporated to dryness in vacuo. The evaporation was repeated several times with addition of EtOH, the remaining oil crystallized from 0.5N HCl in MeOH, the solution evaporated to a small volume, Et2O added, and the resulting crystals recrystd. from

MeOH-Et2O to yield 18.6 g. L-phenylalaninamide, m. 235-7° (decomposition), [α]12D -20.4° (c 2, H2O). Elution of the L-phenylalanine from the column was accomplished with 10 l. 2N HCl and fraction detections by paper chromatography. The fractions were evaporated to dryness in vacuo 3 times to remove excess HCl, the residue dissolved in H2O, neutralized with Et3N, and product recrystd. from hot H2O-EtOH to yield 17.3 g. L-phenyl-alanine, m. 270-3°, [α]12D -34.1° (c 2, H2O). D-Phenylalaninamide-HCl (4.0 g.) was refluxed 5 hrs. with 60 ml. 2N HCl to yield 3.0 g. D-phenylalanine, m. 271-4° (decomposition), [α]9D 33.8° (c 2, H2O), in the usual manner. I was resolved as described above. The incubation mixture was evaporated to a small volume, EtOH added, and the resulting crystals collected and recrystd. from hot H2O-Et2O in 51-5% yield, [α]12D -35.1° (c 2, H2O). The filtrate and washings from the L-amino acid were evaporated to dryness in vacuo and the residue treated the same as D-phenylaminobutyric acid amide hydrochloride to yield 77-81% D-phenylalaninamide, m. 234-7° (decomposition), [α]12D -20.1° (c 2, H2O). To 64.5 g. II.HCl in H2O at pH 7.5, adjusted with NH4OH, was added enzyme equivalent to 0.9 mg. N, the mixture made up to 6 l. with H2O, the solution incubated at 38° after 50 hrs. the mixture cooled, and the resulting crystals washed thoroughly with cold H2O to yield 15.6 g. L-γ-phenyl-α-aminobutyric acid. The filtrate and washings were combined, addnl. enzyme equivalent to 0.6 mg. N added, the volume adjusted to 9 l. and the solution incubated 20 hrs.; results of NH3 detns. indicated complete hydrolysis. The incubation was continued 15 addnl. hrs., the solution evaporated to 150 ml., and the resulting crystals recrystd. from hot dilute HCl-aqueous NH4OH in 24.5 g. yield, m. 310-13° (decomposition), [α]9D 48.1° (c 1, N HCl). The combined filtrate and washings from the L-amino acid were evaporated to dryness in vacuo, 75 ml. 5N NaOH added with cooling, the solution extracted with CHCl3, the extract dried over Na2SO6, evaporated to dryness in vacuo, the oily residue dissolved in 300 ml. 0.5N HCl in MeOH and evaporated to small volume, Et2O added, and the crystals recrystd. from MeOH-Et2O to yield 27.2 g. D-γ-phenyl- α -**aminobutyramide** hydrochloride (VII), m. 253-4° (decomposition), [α]9D -23.7° (c 2, H2O). D-γ-Phenyl-α-aminobutyric acid, m. 308-11° (decomposition), [α]9D -48.7° (c 1, N HCl), was obtained in 96% yield from VII by the same procedure as that for D-phenylalanine. Total results indicate that the products in the digests could be separated conveniently by the use of ion-exchange resin, Amberlite IRA-400 in the case of I, by the differential solubility in the case of II. The D-amino acid amide hydrochlorides obtained were changed to D-amino acids by acid hydrolysis.

AB cf. du Vigneaud and Irish, C.A. 32, 17641. DL-Phenylalaninamide (I) and DL-phenylamino-butyramide (II) were resolved to L-amino acids and D-amino acid amides by partially purified leucine aminopeptidase (III). A partially purified enzyme solution of III was prepared as described by Smith (cf. Spackman, et al., C.A. 49, 4754g). The rate of enzyme action on the amides was followed by measurement of the extent of NH3 liberated in Conway microdiffusion vessels (cf. Johnson, et al., C.A. 45, 3880c). The rate of hydrolysis (Cl + substrate concentration) of I and II with the enzyme preparation slightly increased with increase in concentration of the substrates. In the presence of Mn++) (0.0005 .apprx. 0.008M), an apparent increase of hydrolysis was observed in the case of I, with little corresponding effect with II. I.HCl, m. 234-6°, was synthesized from DL-phenylalanine Et ester-HCl in 95% yield by the method of Smith and Spackman (cf. C.A. 49, 4754h). DL-γ-Phenyl-α-aminobutyric acid (IV) was prepared by refluxing Et acetamidocyanoacetate, Na, and PhCH2CH2Br in EtOH, the precipitated salt filtered off, a small amount of AcOH added, the filtrate evaporated in vacuo to an oil which later crystallized on addition of H2O, the crystals collected, and washed with H2O to yield the Et ester, m.

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could be separated conveniently by the use of ion-exchange resin, Amberlite IRA-400 in the case of I, by the differential solubility in the case of II. The D-amino acid amide hydrochlorides obtained were changed to D-amino acids by acid hydrolysis.

L28 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1959:45632 CAPLUS
DOCUMENT NUMBER: 53:45632
ORIGINAL REFERENCE NO.: 53:8255a-c
TITLE: Resolution of phenylalanine and γ-phenyl-α-aminobutyric acid by leucine aminopeptidase
AUTHOR(S): Tanaka, Atsushi
SOURCE: Fukuoka Igaku Zasshi (1958), 49, 3546-54
CODEN: FKIZA4; ISSN: 0016-254X
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB DL-Phenylalanine amide (I) and DL-γ-phenyl- α - **aminobutyric acid amide** (II) were asymmetrically hydrolyzed by leucine aminopeptidase, obtained by the method of Smith and Spackman (C.A. 49, 4754h), to the corresponding L-amino acids and D-amino acid amides. In the case of I, the hydrolysis proceeded only in the presence of Mn++, while the hydrolysis of II required no Mn++. The yield of L-phenylalanine and D-phenylalanine amide from the hydrolyzate of I was 93 and 82% of the theory, resp., and that of L-γ-phenyl-α-aminobutyric acid and D-γ-phenyl-. **alpha.-aminobutyric acid amide** from II was 84 and 90%, resp. The separation of the isomers was performed by adsorption on Amberlite IRA-400 resin and fractional crystallization
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L28 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1956:11979 CAPLUS
DOCUMENT NUMBER: 50:11979
ORIGINAL REFERENCE NO.: 50:2426g-i,2427a-d
TITLE: The preparation and properties of some amino acid amides
AUTHOR(S): Chambers, Robert W.; Carpenter, Frederick H.
CORPORATE SOURCE: Univ. of California, Berkeley
SOURCE: Journal of the American Chemical Society (1955), 77, 1522-6
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 50:11979
AB cf. C.A. 47, 5354i; following abstract The preparation and properties of the amides of a number of commonly occurring amino acids were studied. The apparent dissociation consts. of the α-amino groups of the amides as well as the paper chromatog. behavior of the amides is reported. Amino acid ester-HCl salts were prepared by the method of Vaughan and Eichler (C.A. 49, 860e). The ester-HCl (5 g.) in 10-15 cc. MeOH decomposed with 1 equivalent Et3N, about 200 cc. Et2O added, the mixture cooled 1 h. in an ice-salt bath, filtered, the filtrate and washings concentrated in vcauo, the

free base kept 3 days in 50 cc. MeOH saturated with NH3, the solvent removed in vacuo, and the residue dried by the evaporation of MeOH and C6H6 yielded the amide which was converted to the acetate. Sirupy L-proline Et ester-HCl yielded the free amide, m. 102-4°; HCl salt, m. 179-81°, [α]D23.5 -68.4° (c 2, EtOH); a crystalline acetate could not be prepared For the compds. prepared, the DL-amino acid, type of ester, m.p. of the ester-HCl, and m.p. and % yield of the amide acetate are: glycine, Et, 145-8°, 122-4°, 69; leucine, Et, 106-10°, 140-1°, 65; valine, Me, 112-13°, 140-3°, 66; phenylalanine, Me, 156-7°, 139-40°, 29; methionine, Me, 109-11°, 143-6°, 27; serine, Me, 133-4°, 117-19°, 57; alanine, Et, 81-3°, 136-7°, 77; tyrosine, Et, 105-6°, 159-61°, 64; tryptophan, Me, 221-2°, 126-7°, 56; histidine, Me, 191-3°, 151-2° (monoacetate), 50; aspartic acid, Me, 111-14°, 136-7°, 54. By the method of Bergmann and Zervas (C.A. 26, 5072) PNBC-aspartic acid (PNBC = p-nitrobenzyloxycarbonyl) (5.0 g.) in 25 cc. Ac2O cooled in an ice-salt bath, and the solution diluted with 75 cc. Et2O followed by 100 cc. petr. ether yielded 3.25 g. PNBC-DL-aspartic anhydride (I), m. 163-4.5°. I (0.968 g.) in 10 cc. EtOH-NH4OH (6.7 cc. concentrated NH4OH diluted to 100 cc. with EtOH) let stand 1 h., 5 cc. water added, and the solution acidified with HCl yielded 0.39 g. PNBC-DL-isoasparagine (II), m. 162-3°. Hydrogenolysis of 2.61 g. II over Pd in EtOH-AcOH (2:1) yielded 0.38 g. isoasparagine. DL-Asparagine (6.6 g.) by the method of Gish and Carpenter (C.A. 48, 1959d) yielded 11.29 g. PNBC-DL-asparagine, m. 159-60°. PNBC-L-glutamic acid (2 g.) in 15 cc. Ac2O heated exactly 5 min. in a boiling water bath and the solvent removed in vacuo yielded 1.70 g. PNBC-L-glutamic anhydride (III), m. 156-8°, [α]D24 -34.2° (c 2.5, dioxane). III (1.5 g.) warmed in 25 cc. dioxane, the solution cooled to room temperature, treated with NH3 gas a few min., the mixture allowed to stand 1.5 h., the solvent removed in vacuo, the salt dissolved in 20 cc. hot water, the solution filtered, acidified with HCl, and cooled rapidly to room temperature yielded 0.645 g. PNBC-L-isoglutamine (IV), m. 166-70° (changed crystal form at 130-5°), [α]D24 4.0° (c 10, HCONMe2). Hydrogenolysis of 200 mg. IV over 40 mg. Pd in 10 cc. 1:1 EtOH-EtOAc yielded 0.120 g. L-isoglutamine (V), m. 171-2°, [α]D24 19.4° (c 3, water). PNBC-L-glutamic acid (5.0 g.) yielded 0.74 g. V, m. 175-6°, [α]D24 20.5° (c 3, water). By the method of Angier, et al. (C.A. 45, 1031a) di-Et L-glutamate, m. 114-16°, [α]D26 21.3° (c 7, EtOH), yielded 12% γ-carbethoxy-L-**alpha.-aminobutyramide** (VI), m. 194-5°, [α]D23 22.8° (c 2, water). VI-HCl (1.0 g.) in 10 cc. HCl (d. 1.188) allowed to stand 2 h. at room temperature, the mixture filtered, yielded 775 mg. L-isoglutamine-HCl, m. 214-16°; free base, m. 173-4°, [α]D24 19.9° (c 3, water).

AB cf. C.A. 47, 5354i; following abstract The preparation and properties of the amides of a number of commonly occurring amino acids were studied. The apparent dissociation consts. of the α-amino groups of the amides as well as the paper chromatog. behavior of the amides is reported. Amino acid ester-HCl salts were prepared by the method of Vaughan and Eichler (C.A. 49, 860e). The ester-HCl (5 g.) in 10-15 cc. MeOH decomposed with 1 equivalent Et3N, about 200 cc. Et2O added, the mixture cooled 1 h. in an ice-salt bath, filtered, the filtrate and washings concentrated in vcauo, the free base kept 3 days in 50 cc. MeOH saturated with NH3, the solvent removed in vacuo, and the residue dried by the evaporation of MeOH and C6H6 yielded the amide which was converted to the acetate. Sirupy L-proline Et ester-HCl yielded the free amide, m. 102-4°; HCl salt, m. 179-81°, [α]D23.5 -68.4° (c 2, EtOH); a crystalline acetate could not be prepared For the compds. prepared, the DL-amino acid, type of ester, m.p. of the ester-HCl, and m.p. and % yield of the amide acetate are: glycine, Et, 145-8°, 122-4°, 69; leucine, Et, 106-10°,

140-1°, 65; valine, Me, 112-13°, 140-3°, 66; phenylalanine, Me, 156-7°, 139-40°, 29; methionine, Me, 109-11°, 143-6°, 27; serine, Me, 133-4°, 117-19°, 57; alanine, Et, 81-3°, 136-7°, 77; tyrosine, Et, 105-6°, 159-61°, 64; tryptophan, Me, 221-2°, 126-7°, 56; histidine, Me, 191-3°, 151-2° (monoacetate), 50; aspartic acid, Me, 111-14°, 136-7°, 54. By the method of Bergmann and Zervas (C.A. 26, 5072) PNBC-aspartic acid (PNBC = p-nitrobenzyloxycarbonyl) (5.0 g.) in 25 cc. Ac2O cooled in an ice-salt bath, and the solution diluted with 75 cc. Et2O followed by 100 cc. petr. ether yielded 3.25 g. PNBC-DL-aspartic anhydride (I), m. 163-4.5°. I (0.968 g.) in 10 cc. EtOH-NH4OH (6.7 cc. concentrated NH4OH diluted to 100 cc. with EtOH) let stand 1 h., 5 cc. water added, and the solution acidified with HCl yielded 0.39 g. PNBC-DL-isoasparagine (II), m. 162-3°. Hydrogenolysis of 2.61 g. II over Pd in EtOH-AcOH (2:1) yielded 0.38 g. isoasparagine. DL-Asparagine (6.6 g.) by the method of Gish and Carpenter (C.A. 48, 1959d) yielded 11.29 g. PNBC-DL-asparagine, m. 159-60°. PNBC-L-glutamic acid (2 g.) in 15 cc. Ac2O heated exactly 5 min. in a boiling water bath and the solvent removed in vacuo yielded 1.70 g. PNBC-L-glutamic anhydride (III), m. 156-8°, [α]D24 -34.2° (c 2.5, dioxane). III (1.5 g.) warmed in 25 cc. dioxane, the solution cooled to room temperature, treated with NH3 gas a few min., the mixture allowed to stand 1.5 h., the solvent removed in vacuo, the salt dissolved in 20 cc. hot water, the solution filtered, acidified with HCl, and cooled rapidly to room temperature yielded 0.645 g. PNBC-L-isoglutamine (IV), m. 166-70° (changed crystal form at 130-5°), [α]D24 4.0° (c 10, HCONMe2). Hydrogenolysis of 200 mg. IV over 40 mg. Pd in 10 cc. 1:1 EtOH-EtOAc yielded 0.120 g. L-isoglutamine (V), m. 171-2°, [α]D24 19.4° (c 3, water). PNBC-L-glutamic acid (5.0 g.) yielded 0.74 g. V, m. 175-6°, [α]D24 20.5° (c 3, water). By the method of Angier, et al. (C.A. 45, 1031a) di-Et L-glutamate, m. 114-16°, [α]D26 21.3° (c 7, EtOH), yielded 12% γ-carbethoxy-L-**alpha.-aminobutyramide** (VI), m. 194-5°, [α]D23 22.8° (c 2, water). VI-HCl (1.0 g.) in 10 cc. HCl (d. 1.188) allowed to stand 2 h. at room temperature, the mixture filtered, yielded 775 mg. L-isoglutamine-HCl, m. 214-16°; free base, m. 173-4°, [α]D24 19.9° (c 3, water).

L28 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1954:903 CAPLUS
DOCUMENT NUMBER:	48:903
ORIGINAL REFERENCE NO.:	48:175e-i,176a-d
TITLE:	The preparation of hydroxypyrazines and derived chloropyrazines
AUTHOR(S):	Karmas, Geo.; Spoerri, Paul E.
CORPORATE SOURCE:	Polytech. Inst. of Brooklyn, Brooklyn, NY
SOURCE:	Journal of the American Chemical Society (1952), 74, 1580-4 CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE:	Journal
LANGUAGE:	Unavailable

GI For diagram(s), see printed CA Issue.

AB Hydroxypyrazines can be synthesized from α-dicarbonyl compds. and hydrohalides of amino acid amides (cf. Jones, C.A. 43, 3009e). α-Bromovaleric and α-bromoisovaleric acids, refluxed 7 hrs. with 50% excess SOCl2 yielded 75-80% acid chlorides, b60 93-5° and b53 84-5, resp. The acid chlorides added dropwise to 28% NH4OH at -30° yielded the amides. The starting material added to 28% NH4OH saturated with NH3 at 0°, yielded the following α-amino acid amide hydrohalides, starting material, product, % yield, and highest m.p. given: ClCH2CONH2, glycine amide-HCl, 85, 203-5°; MeCHClCO2Et,

alanine amide-HCl, 60, 172-3°; MeCHBrCO2Et, alanine amide-HBr, 85, 156-60°; EtCHBrCO2Et, α -**aminobutyramide** -HBr (I), 90, 190-2°; PrCHBrCONH2, norvaline amide-HBr, 76, 218-19°; α-bromoisovaleramide, valine amide-HBr, 70, 233-5°. Condensation of the amides with α-dicarbonyl compds. yielded hydrooxypyrazines (R1, R2, R3, % yield, and m.p. given): H, H, H, 51, 188-90°; H, H, Me, 8, 250-1°; H, Me, H, 27, 126-8°; Me, H, H, 85, 151-2°; H, Me, Me, 30, 201-2°; Me, H, Me, 25, 210-11°; Me, Me, H, 70, 146-7°; Me, Me, Me, 70, 204-5°; Et, H, H, 82, 96-7°; Et, Me, H, 32, 99-100°; Et, Me, Me, 60, 149-50°; Pr, H, H, 80, 79-80°; Pr, Me, H, 60, 75-6°; Pr, Me, Me, 64, 119-20°, iso-Pr, H, H, 46, 76-7°; iso-Pr, Me, H, 30, 91-2°; iso-Pr, Me, Me, 23, 144-5°; H, Ph, Ph, 69, 243-4°; Me, Ph, Ph, 47, 213-14°; Et, Ph, Ph, 46, 207-8°; Pr, Ph, Ph, 60, 205-6°; iso-Pr, Ph, Ph, 47, 234-5°. I with methylglyoxal yielded 4% 2-hydroxy-3-ethyl-6-methylpyrazine, m. 181-2°; Ag salt insol. POCl3 (15 cc.) containing 1 drop H2SO4 and 0.04 mole of the hydroxy compound refluxed, cooled, the mixture poured into 200 g. ice and 100 cc. Et2O, the mixture neutralized with 28% NH4OH, made strongly alkaline with NaOH and extracted with Et2O yielded the chloropyrazines. 2-Chloro-5-methylpyrazine (0.3 g.) and 9 cc. 28% NH4OH heated sealed 20 hrs. at 200°, the solution saturated with NaOH, and extracted with Et2O yielded 2-amino-5-methylpyrazine, m. 117.5-18°. The 6-Me isomer m. 127-8°. 2-chloropyrazines; R1, R2, R3, % Yield, B.p. °C.)/mm., M.p.(°C.) or ntD, t °C.; H, H, H, 65, 62-3/31, 1.5342, 25; H, H, Me, 69, 84-5/40, 50-1, ; H, Me, H, 30, 94-6/60, . ., ; Me, H, H, 65, 94-6/65, 1.5302, 25; H, Me, Me, 60, 86-8/20, 1.5290, 23; Me, H, Me, 26, 112-13/70, 1.5243, 26; Me, Me, H, 67, 111-12/70, 1.5230, 24; Me, Me, Me, 75, 100-1/25, 56-7, ; Et, H, H, 75, 110-11/72, 1.5244, 22; Et, Me, H, 32, 93-4/20, 1.5186, 23; Et, Me, Me, 50, 106-7/20, 1.5205, 25; Pr, H, H, 53, 124-5/65, 1.5144, 24; Pr, Me, H, 77, 106-7/20, 1.5130, 22; Pr, Me, Me, 36, 121-2/20, 1.5147, 24; iso-Pr, H, H, 60, 112-13/65, 1.5104, 25; iso-Pr, Me, H, 76, 95-6/18, 1.5092, 25; iso-Pr, Me, Me, 65, 105-6/15, 1.5120, 25; H, Ph, Ph, 70, 140-5/0.001, 126-7, ; Me, Ph, Ph, 84, 140-50/0.001 , 136-7, ; Et, Ph, Ph, 85, 145-50/0.001 , 77-8, ; Pr, Ph, Ph, 97, 155-60/0.001, . ., ; iso-Pr, Ph, Ph, 75, 155-60/0.001, 96-7

AB Hydroxypyrazines can be synthesized from α-dicarbonyl compds. and hydrohalides of amino acid amides (cf. Jones, C.A. 43, 3009e). α-Bromovaleric and α-bromoisovaleric acids, refluxed 7 hrs. with 50% excess SOCl2 yielded 75-80% acid chlorides, b60 93-5° and b53 84-5, resp. The acid chlorides added dropwise to 28% NH4OH at -30° yielded the amides. The starting material added to 28% NH4OH saturated with NH3 at 0°, yielded the following α-amino acid amide hydrohalides, starting material, product, % yield, and highest m.p. given: ClCH2CONH2, glycine amide-HCl, 85, 203-5°; MeCHClCO2Et, alanine amide-HCl, 60, 172-3°; MeCHBrCO2Et, alanine amide-HBr, 85, 156-60°; EtCHBrCO2Et, α -**aminobutyramide** -HBr (I), 90, 190-2°; PrCHBrCONH2, norvaline amide-HBr, 76, 218-19°; α-bromoisovaleramide, valine amide-HBr, 70, 233-5°. Condensation of the amides with α-dicarbonyl compds. yielded hydrooxypyrazines (R1, R2, R3, % yield, and m.p. given): H, H, H, 51, 188-90°; H, H, Me, 8, 250-1°; H, Me, H, 27, 126-8°; Me, H, H, 85, 151-2°; H, Me, Me, 30, 201-2°; Me, H, Me, 25, 210-11°; Me, Me, H, 70, 146-7°; Me, Me, Me, 70, 204-5°; Et, H, H, 82, 96-7°; Et, Me, H, 32, 99-100°; Et, Me, Me, 60, 149-50°; Pr, H, H, 80, 79-80°; Pr, Me, H, 60, 75-6°; Pr, Me, Me, 64, 119-20°, iso-Pr, H, H, 46, 76-7°; iso-Pr, Me, H, 30, 91-2°; iso-Pr, Me, Me, 23, 144-5°; H, Ph, Ph, 69, 243-4°; Me, Ph, Ph, 47, 213-14°; Et, Ph, Ph, 46, 207-8°; Pr, Ph, Ph, 60, 205-6°; iso-Pr, Ph, Ph, 47,

234-5°. I with methylglyoxal yielded 4% 2-hydroxy-3-ethyl-6-methylpyrazine, m. 181-2°; Ag salt insol. POCl3 (15 cc.) containing 1 drop H2SO4 and 0.04 mole of the hydroxy compound refluxed, cooled, the mixture poured into 200 g. ice and 100 cc. Et2O, the mixture neutralized with 28% NH4OH, made strongly alkaline with NaOH and extracted with Et2O yielded the chloropyrazines. 2-Chloro-5-methylpyrazine (0.3 g.) and 9 cc. 28% NH4OH heated sealed 20 hrs. at 200°, the solution saturated with NaOH, and extracted with Et2O yielded 2-amino-5-methylpyrazine, m. 117.5-18°. The 6-Me isomer m. 127-8°. 2-chloropyrazines; R1, R2, R3, % Yield, B.p. °C.)/mm., M.p.(°C.) or ntD, t °C.; H, H, H, 65, 62-3/31, 1.5342, 25; H, H, Me, 69, 84-5/40, 50-1, ; H, Me, H, 30, 94-6/60, . ., ; Me, H, H, 65, 94-6/65, 1.5302, 25; H, Me, Me, 60, 86-8/20, 1.5290, 23; Me, H, Me, 26, 112-13/70, 1.5243, 26; Me, Me, H, 67, 111-12/70, 1.5230, 24; Me, Me, Me, 75, 100-1/25, 56-7, ; Et, H, H, 75, 110-11/72, 1.5244, 22; Et, Me, H, 32, 93-4/20, 1.5186, 23; Et, Me, Me, 50, 106-7/20, 1.5205, 25; Pr, H, H, 53, 124-5/65, 1.5144, 24; Pr, Me, H, 77, 106-7/20, 1.5130, 22; Pr, Me, Me, 36, 121-2/20, 1.5147, 24; iso-Pr, H, H, 60, 112-13/65, 1.5104, 25; iso-Pr, Me, H, 76, 95-6/18, 1.5092, 25; iso-Pr, Me, Me, 65, 105-6/15, 1.5120, 25; H, Ph, Ph, 70, 140-5/0.001, 126-7, ; Me, Ph, Ph, 84, 140-50/0.001 , 136-7, ; Et, Ph, Ph, 85, 145-50/0.001 , 77-8, ; Pr, Ph, Ph, 97, 155-60/0.001, . ., ; iso-Pr, Ph, Ph, 75, 155-60/0.001, 96-7

L28 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1951:6032 CAPLUS
DOCUMENT NUMBER: 45:6032
ORIGINAL REFERENCE NO.: 45:1031a-i
TITLE: Pteroic acid derivatives. VI. Unequivocal syntheses of some isomeric glutamic acid peptides
AUTHOR(S): Angier, R. B.; Waller, C. W.; Hutchings, B. L.; Boothe, J. H.; Mowat, J. H.; Semb, J.; SubbaRow, Y.
CORPORATE SOURCE: Lederle Labs., Pearl River, NY
SOURCE: Journal of the American Chemical Society (1950), 72, 74-7
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. C.A. 44, 639a. l-2-Oxo-5-pyrrolidinecarboxylic acid (I) (10 g.) and 50 cc. EtOH saturated with HCl, refluxed 1 hr. on the steam bath, and concentrated in vacuo yielded 6.0 g. di-Et glutamate-HCl, m. 113-14°, [α]D 22.4° (c 4, water). Di-Et glutamate (Ia) (238.0 g.) in 290 cc. concentrated NH4OH let stand at room temperature 5 hrs. yielded 112.0 g. l-2-oxo-5-pyrrolidinecarboxamide (II), m. 166-8°, [α]D -42.25° (c 2, water). II (100 g.) and 675 cc. absolute EtOH containing 37.5 g. HCl refluxed 30-40 min. yielded 50.0 g. γ-carbethoxy-. **alpha.-aminobutyramide**-HCl (Et isoglutaminate-HCl) (III), m. 197-8°, [α]26D 21.2° (c 2, water). III Et ester (30.0 g.) added to 400 cc. EtOAc and 40 cc. Et3N, the mixture filtered, 30 g. p-O2NC6H4COCl added, and the mixture allowed to stand 2 hrs. at room temperature and 2 hrs. at 5° yielded 39.5 g. Et (p-nitrobenzoyl)isoglutaminate, O2NC6H4CONHCH(CONH2)CH2CH2COR, (IV, R = OEt), glistening white platelets from absolute EtOH, m. 186-8°, [α]25D 11.75° (c 2, AcOH). IV (14.0 g.) in 80 cc. 100% N2H4.H2O yielded 9.2 g. γ-(p-nitrobenzoyl)isoglutamine hydrazide (V) (IV, R = N2H3), m. 185-7° (from absolute EtOH). Concentrated HCl (12 cc.) with 8.0 g. V in 80 cc. water and 20 cc. EtOAc (ice bath) yielded 7.5-8 g. of the γ-azide (VI). III (11.0 g.) stirred with 200 cc. EtOAc and 16 cc. Et3N, the mixture filtered, and VI from 8 g. V added, yielded 6.3 g. Et [(p-nitrobenzoyl)isoglutaminyl]isoglutaminate (VII), p-O2NC6H4CONHCH(CONH2)CH2CH2CONHCH(COR)CH2CH2COR' (R = NH2, R' = OEt), m. 223-4° (from water), [α]28D 8.5° (c 2, AcOH). Ia (8

cc.) and VI from 2.7 g. V in 75 cc. EtOAc were shaken 90 min. at room temperature and the mixture cooled in an ice bath, yielding 2.5 g. di-Et analog (VIII) of VII (R = OEt), m. 193-4°, [α]25D 8.75° (c 2, AcOH). VIII hydrolyzed with N NaOH for 2 hrs. at 40-50° yielded the acid, m. 194-5° (from water). Et3N (6 cc.) added 7.6 g. tri-Et γ-glutamylglutamate-HCl in 75 cc. EtOAc, the mixture filtered, the VI from 3.0 g. V added, and the mixture cooled to 5° after standing 2 hrs. at room temperature, yielded 4.2 g. tri-Et [(p-nitrobenzoyl)isoglutaminyl]-γ-glutamylglutamate [VII, R = OEt, R' = NHCH(CO2Et)CH2CH2CO2Et] m. 193-4°, [α]27D 4.5° (c 2, AcOH). I Et ester (216.0 g.) in 500 cc. absolute EtOH containing 70 cc. 100% N2H4.H2O warmed to 40° and then allowed to stand at room temperature for 1 day and refrigerated, yielded 175 g. hydrazide (IX), m. 114-15°, [α]28D -11.75° (c 2, water). Concentrated HCl (95 cc.) was added to 75 g. IX in 125 cc. water (ice bath), then 33 g. NaNO2 in 75 cc. water, yielding the azide (X), which could not be isolated with ordinary solvents. X added to 161 g. Ia and 200 g. NaHCO3 in 400 cc. water (5-10°) yielded 30.5 g. di-Et α-(2-oxo-5-pyrrolidine carboxamido)glutarate (XI), m. 132-4° (from EtOAc), [α]29D -40.3° (c 4, water). XI (4 g.) in 15 cc. absolute EtOH containing 0.6 g. HCl was refluxed 1 hr., concentrated to a sirup in vacuo, the sirup dissolved in 35 cc. EtOAc containing 2.0 g. Et3N, the mixture filtered, 4.3 g. p-O2NC6H4COCl added, and the mixture allowed to stand at room temperature 2 hrs. and cooled, yielding 2.7 g. tri-Et N-[N-(p-nitrobenzoyl)-α-glutamyl]glutamate, m. 148-9°, [α]28D 2.76° (c 2, AcOH) ([α]26D 3.25° when prepared directly from the acid). XI (23.3 g.) in 80 cc. absolute EtOH containing 3.5 g. dry HCl refluxed 1 hr., the mixture concentrated to a sirup in vacuo, the sirup dissolved in EtOAc, again concentrated, the sirup (tri-Et N-glutamylglutamate-HCl) dissolved in 40 cc. water containing 30 g. NaHCO3, X (in 50 cc. water) from 7.25 IX added, and the mixture stirred 3 hrs. at room temperature and cooled, yielded 3.8 g. Et γ-(2-oxo-5-pyrrolidylcarboxamido)-N-(1,3-dicarbethoxypropyl)glutaramate, HN.CO.CH2.CH2.CHCONHCH(CH2CH2CO2Et)CONHCH(CO2Et)CH2CH2CO2Et (XII), m. 133-5° (softens at 117°). XII (3.5 g.) and 15 cc. absolute alc. containing 0.34 g. HCl refluxed 1 hr. yielded 1.5 g. tetra-Et N-{N-[N-(p-nitrobenzoyl)-α-glutamyl]-α-glutamyl}glutamate (XIII), m. 114-15° (from EtOH). Another form of XIII m. 147-8°.

AB cf. C.A. 44, 639a. l-2-Oxo-5-pyrrolidinecarboxylic acid (I) (10 g.) and 50 cc. EtOH saturated with HCl, refluxed 1 hr. on the steam bath, and concentrated in vacuo yielded 6.0 g. di-Et glutamate-HCl, m. 113-14°, [α]D 22.4° (c 4, water). Di-Et glutamate (Ia) (238.0 g.) in 290 cc. concentrated NH4OH let stand at room temperature 5 hrs. yielded 112.0 g. l-2-oxo-5-pyrrolidinecarboxamide (II), m. 166-8°, [α]D -42.25° (c 2, water). II (100 g.) and 675 cc. absolute EtOH containing 37.5 g. HCl refluxed 30-40 min. yielded 50.0 g. γ-carbethoxy-**alpha.-aminobutyramide**-HCl (Et isoglutaminate-HCl) (III), m. 197-8°, [α]26D 21.2° (c 2, water). III Et ester (30.0 g.) added to 400 cc. EtOAc and 40 cc. Et3N, the mixture filtered, 30 g. p-O2NC6H4COCl added, and the mixture allowed to stand 2 hrs. at room temperature and 2 hrs. at 5° yielded 39.5 g. Et (p-nitrobenzoyl)isoglutaminate, O2NC6H4CONHCH(CONH2)CH2CH2COR, (IV, R = OEt), glistening white platelets from absolute EtOH, m. 186-8°, [α]25D 11.75° (c 2, AcOH). IV (14.0 g.) in 80 cc. 100% N2H4.H2O yielded 9.2 g. γ-(p-nitrobenzoyl)isoglutamine hydrazide (V) (IV, R = N2H3), m. 185-7° (from absolute EtOH). Concentrated HCl (12 cc.) with 8.0 g. V in 80 cc. water and 20 cc. EtOAc (ice bath) yielded 7.5-8 g. of the γ-azide (VI). III (11.0 g.) stirred with 200 cc. EtOAc and

16 cc. Et3N, the mixture filtered, and VI from 8 g. V added, yielded 6.3 g. Et [(p-nitrobenzoyl)isoglutaminyl]isoglutaminate (VII), p-O2NC6H4CONHCH(CONH2)CH2CH2CONHCH(COR)CH2CH2COR' (R = NH2, R' = OEt), m. 223-4° (from water), [α]28D 8.5° (c 2, AcOH). Ia (8 cc.) and VI from 2.7 g. V in 75 cc. EtOAc were shaken 90 min. at room temperature and the mixture cooled in an ice bath, yielding 2.5 g. di-Et analog (VIII) of VII (R = OEt), m. 193-4°, [α]25D 8.75° (c 2, AcOH). VIII hydrolyzed with N NaOH for 2 hrs. at 40-50° yielded the acid, m. 194-5° (from water). Et3N (6 cc.) added 7.6 g. tri-Et γ-glutamylglutamate-HCl in 75 cc. EtOAc, the mixture filtered, the VI from 3.0 g. V added, and the mixture cooled to 5° after standing 2 hrs. at room temperature, yielded 4.2 g. tri-Et [(p-nitrobenzoyl)isoglutaminyl]-γ-glutamylglutamate [VII, R = OEt, R' = NHCH(CO2Et)CH2CH2CO2Et] m. 193-4°, [α]27D 4.5° (c 2, AcOH). I Et ester (216.0 g.) in 500 cc. absolute EtOH containing 70 cc. 100% N2H4.H2O warmed to 40° and then allowed to stand at room temperature for 1 day and refrigerated, yielded 175 g. hydrazide (IX), m. 114-15°, [α]28D -11.75° (c 2, water). Concentrated HCl (95 cc.) was added to 75 g. IX in 125 cc. water (ice bath), then 33 g. NaNO2 in 75 cc. water, yielding the azide (X), which could not be isolated with ordinary solvents. X added to 161 g. Ia and 200 g. NaHCO3 in 400 cc. water (5-10°) yielded 30.5 g. di-Et α-(2-oxo-5-pyrrolidine carboxamido)glutarate (XI), m. 132-4° (from EtOAc), [α]29D -40.3° (c 4, water). XI (4 g.) in 15 cc. absolute EtOH containing 0.6 g. HCl was refluxed 1 hr., concentrated to a sirup in vacuo, the sirup dissolved in 35 cc. EtOAc containing 2.0 g. Et3N, the mixture filtered, 4.3 g. p-O2NC6H4COCl added, and the mixture allowed to stand at room temperature 2 hrs. and cooled, yielding 2.7 g. tri-Et N-[N-(p-nitrobenzoyl)-α-glutamyl]glutamate, m. 148-9°, [α]28D 2.76° (c 2, AcOH) ([α]26D 3.25° when prepared directly from the acid). XI (23.3 g.) in 80 cc. absolute EtOH containing 3.5 g. dry HCl refluxed 1 hr., the mixture concentrated to a sirup in vacuo, the sirup dissolved in EtOAc, again concentrated, the sirup (tri-Et N-glutamylglutamate-HCl) dissolved in 40 cc. water containing 30 g. NaHCO3, X (in 50 cc. water) from 7.25 IX added, and the mixture stirred 3 hrs. at room temperature and cooled, yielded 3.8 g. Et γ-(2-oxo-5-pyrrolidylcarboxamido)-N-(1,3-dicarbethoxypropyl)glutaramate, HN.CO.CH2.CH2.CHCONHCH(CH2CH2CO2Et)CONHCH(CO2Et)CH2CH2CO2Et (XII), m. 133-5° (softens at 117°). XII (3.5 g.) and 15 cc. absolute alc. containing 0.34 g. HCl refluxed 1 hr. yielded 1.5 g. tetra-Et N-{N-[N-(p-nitrobenzoyl)-α-glutamyl]-α-glutamyl}glutamate (XIII), m. 114-15° (from EtOH). Another form of XIII m. 147-8°.

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	124.80	382.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-27.01	-51.58

FILE 'REGISTRY' ENTERED AT 10:42:26 ON 21 MAR 2005

Property values tagged with IC are from the ZIC/VINITI data file

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STRUCTURE FILE UPDATES: 20 MAR 2005 HIGHEST RN 845957-95-1
DICTIONARY FILE UPDATES: 20 MAR 2005 HIGHEST RN 845957-95-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> s ethyl-2-oxo-1-pyrrolidineacetamide/cn; d
L29 0 ETHYL-2-OXO-1-PYRROLIDINEACETAMIDE/CN

L29 HAS NO ANSWERS
L29 0 SEA FILE=REGISTRY ABB=ON PLU=ON ETHYL-2-OXO-1-PYRROLIDINEACETAMIDE/CN

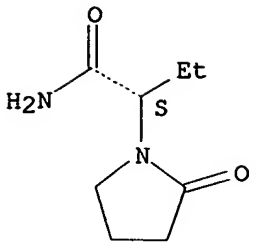
=> s levetiracetam
L30 1 LEVETIRACETAM

=> s levetiracetam/cn
L31 1 LEVETIRACETAM/CN

=> d L31

L31 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 102767-28-2 REGISTRY
ED Entered STN: 21 Jun 1986
CN 1-Pyrrolidineacetamide, α-ethyl-2-oxo-, (αS)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Pyrrolidineacetamide, α-ethyl-2-oxo-, (S)-
OTHER NAMES:
CN Keppra
CN **Levetiracetam**
CN UCB-L 059
FS STEREOSEARCH
MF C8 H14 N2 O2
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, DIOGENES, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

212 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
212 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> FIL REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	17.36	399.69

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-51.58

FILE 'REGISTRY' ENTERED AT 10:44:46 ON 21 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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STRUCTURE FILE UPDATES: 20 MAR 2005 HIGHEST RN 845957-95-1
DICTIONARY FILE UPDATES: 20 MAR 2005 HIGHEST RN 845957-95-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> SET TERMSET E#

SET COMMAND COMPLETED

=> DEL SEL Y

=> SEL L31 1 RN

E1 THROUGH E1 ASSIGNED

```
=>  S E1/RN

L32          1 102767-28-2/RN

=>  SET TERMSET LOGIN

SET COMMAND COMPLETED

=>  FIL USPATFULL

COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.51     400.20

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)            SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00     -51.58

FILE 'USPATFULL' ENTERED AT 10:44:50 ON 21 MAR 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 17 Mar 2005 (20050317/PD)
FILE LAST UPDATED: 17 Mar 2005 (20050317/ED)
HIGHEST GRANTED PATENT NUMBER: US6868552
HIGHEST APPLICATION PUBLICATION NUMBER: US2005060780
CA INDEXING IS CURRENT THROUGH 17 Mar 2005 (20050317/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 17 Mar 2005 (20050317/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2005

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to          <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.
'BI,IT,ST,CC' IS DEFAULT SEARCH FIELD FOR 'USPATFULL' FILE

=>  S L32

L33          27 L32

=> d L33 ti,in,pi

L33  ANSWER 1 OF 27  USPATFULL on STN
TI     Methods of treating non-inflammatory gastrointestinal tract disorders
```

using Cav2.2 subunit calcium channel modulators
IN Fraser, Matthew Oliver, Apex, NC, UNITED STATES
Landau, Steven B., Wellesley, MA, UNITED STATES
Burgard, Edward C., Chapel Hill, NC, UNITED STATES
PI US 2005026835 A1 20050203

=> d L33 ti,in,pi 1-27

L33 ANSWER 1 OF 27 USPATFULL on STN
TI Methods of treating non-inflammatory gastrointestinal tract disorders using Cav2.2 subunit calcium channel modulators
IN Fraser, Matthew Oliver, Apex, NC, UNITED STATES
Landau, Steven B., Wellesley, MA, UNITED STATES
Burgard, Edward C., Chapel Hill, NC, UNITED STATES
PI US 2005026835 A1 20050203

L33 ANSWER 2 OF 27 USPATFULL on STN
TI Combinations of GABA modulators and anticonvulsants, and atypical antipsychotics
IN Romano, Steven Joseph, New York, NY, UNITED STATES
PI US 2005004106 A1 20050106

L33 ANSWER 3 OF 27 USPATFULL on STN
TI Process for producing levetiracetam
IN Dolitzky, Ben-Zion, Petah Tiqva, ISRAEL
Hildesheim, Jean, Mazkeret Batya, ISRAEL
Finogueev, Serguei, Qiriat Arabaa, ISRAEL
PI US 2004259933 A1 20041223

L33 ANSWER 4 OF 27 USPATFULL on STN
TI Use of 2-oxo-1-pyrrolidine derivatives for the preparation of a drug
IN Grimee, Renee, Bruxelles, BELGIUM
Klitgaard, Henrik, Bruxelles, BELGIUM
PI US 2004242671 A1 20041202

L33 ANSWER 5 OF 27 USPATFULL on STN
TI Oxopyrrolidine compounds, preparations of said compounds and their use in the manufacturing of levetiracetam and analogues
IN Ates, Celal, Louvain-la-Neuve, BELGIUM
Surtees, John, Jezus-Eik, BELGIUM
Burteau, Anne-Catherine, Grand-Leez (Gembloux), BELGIUM
Marmon, Violeta, Abingdon-Oxon, UNITED KINGDOM
Cavoy, Emile, Hams-sur-Heure, BELGIUM
PI US 2004204476 A1 20041014

L33 ANSWER 6 OF 27 USPATFULL on STN
TI Methods for the identification of agents for the treatment of seizures, neurological diseases, endocrinopathies and hormonal diseases
IN Lynch, Berkley, Cambridge, MA, UNITED STATES
Nocka, Karl, Cambridge, MA, UNITED STATES
Fuks, Bruno, Brussels, BELGIUM
PI US 2004204388 A1 20041014

L33 ANSWER 7 OF 27 USPATFULL on STN
TI Methods for treating lower urinary tract disorders and the related disorders vulvodynia and vulvar vestibulitis using Cav2.2 subunit calcium channel modulators
IN Fraser, Matthew Oliver, Apex, NC, UNITED STATES
Thor, Karl Bruce, Morrisville, NC, UNITED STATES
Burgard, Edward C., Chapel Hill, NC, UNITED STATES
PI US 2004198775 A1 20041007

L33 ANSWER 8 OF 27 USPATFULL on STN
TI Controlled release modifying complex and pharmaceutical compositions thereof
IN Kannan, Muthaiyyan Esakki, Mumbai, INDIA
Krishnan, Anandi, Mumbai, INDIA
Sapre, Beena Amol, Mumbai, INDIA
Shah, Chitra Siddharth, Mumbai, INDIA
Patil, Atul Vishvanath, Mumbai, INDIA
PI US 2004185097 A1 20040923

L33 ANSWER 9 OF 27 USPATFULL on STN
TI Pharmaceutical composition containing oxcarbazepine and having a controlled active substance release
IN Franke, Hanshermann, Tangstedt, GERMANY, FEDERAL REPUBLIC OF
Lennartz, Peter, Hamburg, GERMANY, FEDERAL REPUBLIC OF
PI US 2004185095 A1 20040923

L33 ANSWER 10 OF 27 USPATFULL on STN
TI Pharmaceutical composition, containing oxcarbazepine with sustained release of an active-ingredient
IN Franke, Hanshermann, Tangstedt, GERMANY, FEDERAL REPUBLIC OF
Lennartz, Peter, Hamburg, GERMANY, FEDERAL REPUBLIC OF
PI US 2004142033 A1 20040722

L33 ANSWER 11 OF 27 USPATFULL on STN
TI Use of levetiracetam for treating or preventing acute headaches
IN Krusz, John Claude, Dallas, TX, UNITED STATES
PI US 2004116506 A1 20040617

L33 ANSWER 12 OF 27 USPATFULL on STN
TI Treatment of tics, tremors and related disorders
IN Krauss, Gregory, Baltimore, MD, UNITED STATES
Singer, Harvey, Baltimore, MD, UNITED STATES
PI US 2004116505 A1 20040617

L33 ANSWER 13 OF 27 USPATFULL on STN
TI Methods for the identification of agents for the treatment of seizures, neurological diseases, endocrinopathies and hormonal diseases
IN Lynch, Berkley, Cambridge, MA, UNITED STATES
Nocka, Karl, Harvard, MA, UNITED STATES
Fuks, Bruno, Brussels, BELGIUM
PI US 2004106147 A1 20040603

L33 ANSWER 14 OF 27 USPATFULL on STN
TI Use of certain substituted pyrrolidones such as piracetam in the treatment of viral and other diseases
IN Peuvot, Jacques, Bousval, BELGIUM
Brasseur, Robert, Haillot, BELGIUM
DeLeers, Michel, Linkebeek, BELGIUM
Pontes, Fausto A, Coimbra, PORTUGAL
Ruysschaert, Jean-Marie, Rhode St Genese, BELGIUM
PI US 2004092575 A1 20040513

L33 ANSWER 15 OF 27 USPATFULL on STN
TI Definitive medications for treating fibromyalgia
IN Benja-Athon, Anuthep, New York, NY, UNITED STATES
PI US 2004092504 A1 20040513

L33 ANSWER 16 OF 27 USPATFULL on STN
TI Neuro-degenerative inhibitor, neuro-endocrine modulator, and neuro-cerebral metabolism enhancer
IN Sassover, Nathan, Los Angeles, CA, UNITED STATES
PI US 2004067986 A1 20040408

L33 ANSWER 17 OF 27 USPATFULL on STN
TI Method for treatment of disorders of personal attachment and deficient social interaction
IN Daniel, David Gordon, McLean, VA, UNITED STATES
PI US 2004058997 A1 20040325

L33 ANSWER 18 OF 27 USPATFULL on STN
TI Use of matrix metalloproteinase inhibitors to mitigate nerve damage
IN Noble, Linda Jeanne, San Francisco, CA, UNITED STATES
Donovan, Frances Muriel, San Francisco, CA, UNITED STATES
Werb, Zena, San Francisco, CA, UNITED STATES
PI US 2003139332 A1 20030724

L33 ANSWER 19 OF 27 USPATFULL on STN
TI Diagnositc methods for determining susceptibility to convulsive conditions
IN Campbell, Allyson J., Kingston, CANADA
Weaver, Donald F., Halifax, CANADA
Lyon, Angela P., Kingston, CANADA
Carran, John R., Kingston, CANADA
PI US 2003077833 A1 20030424

L33 ANSWER 20 OF 27 USPATFULL on STN
TI Buccal, polar and non-polar spray or capsule containing drugs for treating disorders of the central nervous system
IN Dugger, Harry A., III, Flemington, NJ, UNITED STATES
PI US 2003077227 A1 20030424

L33 ANSWER 21 OF 27 USPATFULL on STN
TI Methods and compositions for treating conditions of the central and peripheral nervous systems using non-synaptic mechanisms
IN Hochman, Daryl W., Bahama, NC, UNITED STATES
PI US 2002082252 A1 20020627

L33 ANSWER 22 OF 27 USPATFULL on STN
TI Process for preparing (s)- and (R)-α-ethyl-2-oxo-1-pyrrolidineacetamide
IN Cavoy, Emile, Ham-sur-Heure, Belgium
Hamende, Michel, Uccle, Belgium
Deleers, Michel, Linkebeek, Belgium
Canvat, Jean-Pierre, Brussels, Belgium
Zimmermann, Vincent, Brussels, Belgium
PI US 6124473 20000926

L33 ANSWER 23 OF 27 USPATFULL on STN
TI Process for the preparation of levetiracetam
IN Futagawa, Tooru, Hyogo, Japan
Canvat, Jean-Pierre, Brussels, Belgium
Cavoy, Emile, Ham-Sur-Heure, Belgium
Deleers, Michel, Linkebeek, Belgium
Hamende, Michel, Uccle, Belgium
Zimmermann, Vincent, Brussels, Belgium
PI US 6107492 20000822

L33 ANSWER 24 OF 27 USPATFULL on STN
TI Treatment of anxiety with the aid of (S)-(-)-α-ethyl-2-oxo-1-pyrrolidineacetamide
IN Wulfert, Ernst, Brussels, Belgium
Gobert, Jean, Brussels, Belgium
Gower, Alma, Braine-l'Alleud, Belgium
Cossement, Eric, Brussels, Belgium
PI US 5447952 19950905

L33 ANSWER 25 OF 27 USPATFULL on STN
TI (S)-alpha-ethyl-2-oxo-1-pyrrolidineacetamide
IN Gobert, Jean, Brussels, Belgium
Geerts, Jean-Pierre, Leglise, Belgium
Bodson, Guy, Bellefontaine, Belgium
PI US 4943639 19900724

L33 ANSWER 26 OF 27 USPATFULL on STN
TI (S)-alpha-ethyl-2-oxo-1-pyrrolidineacetamide compositions
IN Gobert, Jean, Brussels, Belgium
Geerts, Jean-Pierre, Leglise, Belgium
Dodson, Guy, Bellefontaine, Belgium
PI US 4837223 19890606

L33 ANSWER 27 OF 27 USPATFULL on STN
TI (S)-alpha-ethyl-2-oxo-1-pyrrolidineacetamide
IN Gobert, Jean, Brussels, Belgium
Geerts, Jean-Pierre, Leglise, Belgium
Bodson, Guy, Bellefontaine, Belgium
PI US 4696943 19870929

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	28.30	428.50

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-51.58

STN INTERNATIONAL LOGOFF AT 10:45:28 ON 21 MAR 2005